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By H. S. Raper, C.B.E., D.Sc., M.B. Leeds, F.R.S.,
BRACKENBURY PROFESSOR OF PHYSIOLOGY IN THE UNIVERSITY OF MANCHESTER.

Unlike the chemist, the animal cell has a very limited choice of raw materials from which synthesis must start. These are the components of the common foodstuffs. When they have undergone the preliminary processes of digestion they provide in all about 30 substances which may be regarded as available for the building up of new compounds by the cell. They consist of about 20 amino-acids, two purine bases, three pyrimidine bases, three hexoses, glycerol, and higher fatty acids. It is true that there may be other hitherto undiscovered components of foodstuffs which are important as raw material for synthesis in the animal cell, but they can be but few in number and present in small amount.

Substances Synthetised from Unidentified Raw Materials.

Given this list of raw materials can we indicate which is the likely starting-point for the synthesis of substances whose constitution is known or partly known? This question must still be answered in the negative for such well-known products as cholesterol and the unconjugated acids of bile. It is possible that the experiments of Channon, who demonstrated that addition of spinacene to the diet of rats caused the cholesterol content of the liver to increase to double its usual amount, may afford a clue to the origin of this substance, but it is difficult to conceive of spinacene being the raw material for this synthesis in the herbivorous animal. As for the bile-acids, we are in complete ignorance of the substance or substances from which they are built up. The probable raw material for the synthesis of the purine bases, which are components of nuclear material and therefore present in all cells, must also be answered in the negative, but with less emphasis than in the case of cholesterol and the bile-acids. The amino-acid histidin, which contains a five-membered ring similar to that found in the purine bases, is their most likely precursor on structural grounds. The synthesis of cholesterol, that of the bile-acids, and of purine bases are still problems in the purely chemical sense. When the chemist has indicated their likely solution it will be the task of physiology to find out the mechanism by which the cell brings about the necessary chemical processes.

An example of a synthetic product which bears a fairly close structural relationship to two of the amino-acids which are found in proteins is adrenalin. These two amino-acids, phenylalanin and tyrosin, have practically the same carbon skeleton as adrenalin. Either of them might give rise to adrenalin by successive oxidation, methylation of the amino group, and loss of carbon dioxide. That a part of the necessary oxidation process can be brought about by means of an oxidising enzyme has already been demonstrated. This enzyme, tyrosinase, will oxidise tyrosin to 3 : 4-dihydroxyphenylalanin. It is, therefore, conceivable that the first stage of the synthesis from tyrosin occurs in this way in the cell. If, however, we consider how we may find out whether a process of this kind, operating in the cells of the adrenal gland under specific conditions, gives rise to adrenalin, many difficulties appear. The discovery of the mechanisms by which adrenalin is formed, although a simple problem at first sight, is probably in reality very complicated.

The case of thyroxin is comparable with that of adrenalin. Thyroxin is a relatively simple chemical substance which could conceivably be produced by the oxidation of diiodotyrosin. The last-named compound has recently been shown to be present in the thyroid gland and this makes the presumption that it is the mother substance of thyroxin all the stronger. Yet it has not been demonstrated either in vitro or in vivo that thyroxin may be produced from diiodotyrosin.

These two instances of adrenalin and thyroxin show that, even when there is a reasonable presumption that we know the raw material from which the synthesis in the cell starts and the chemical processes concerned, the proof that our hypotheses are correct is far from simple.

Substances Synthetised from known Raw Materials by unknown Chemical Reactions.

We may now pass on to consider a process in which the raw material is known with certainty but the chemical reactions by which the synthesis takes place are relatively obscure—the production of fat from carbohydrate. Lawes and Gilbert, in their classical experiments at Rothamsted on the fattening of farm stock, showed indubitably that animals can produce fat from starch. It has been confirmed since by others. Since the starch is converted into glucose in the alimentary canal prior to absorption we may consider glucose as the starting-point of the synthesis.

The evidence for the mechanism of synthesis of the fatty acids from some simple reactive substance which is first produced by degradation of glucose, such as acetaldehyde or pyruvic acid, is purely chemical and the grounds on which it can be put forward are largely chemical ones. Is there any physiological support for this scheme? Studies of the synthesis of fat in animals have yielded very little so far. It is, however, known that acetaldehyde and pyruvic acid, the intermediates postulated in the hypothesis just mentioned, can be produced in the body. When we know what the conditions are which set the process of fat synthesis going, and when we are able to reproduce them at will in animals, it may be possible to determine what are the intermediate substances concerned.

More success has been achieved by a study of the formation of fatty acids in micro-organisms, some of which possess this faculty in a remarkable degree. Bacteria which form butyric acid from glucose have been found to produce in addition both lactic acid and acetaldehyde. These same bacteria will also produce butyric acid from pyruvic aldol though not from aldehyde ammonia, aldol, or pyruvic acid itself. It appears probable that the processes by which these lower members of the series of fatty acids are formed in bacterial fermentation may be the same as those by which higher members of the series are formed in animals. The production of fat is a process which is common to a great variety of living organisms, both simple and complex, animal and vegetable. It is not

* Abridged from an address delivered to the section of Physiology of the British Association for the Advancement of Science on Sept. 4th.

unlikely, therefore, to be carried out by the same series of chemical reactions wherever it is found. It may be that we shall eventually discover the reactions responsible for the synthesis of fat in animals by investigating the processes by which it occurs in vegetable forms, such as bacteria or moulds.

Syntheses from known Raw Materials by partially known Chemical Processes.

We have also to consider how the synthetic product is dealt with in the cell so as to protect it from the disruptive agencies which exist there. Arrangements for this purpose must be present, since we know that substances may accumulate in cells which contain enzymes that hydrolyse them. For example, fat and lipase coexist in the liver cell and also glycogen and amylase. The phenomena of autolysis illustrate the same fact too. Whatever these arrangements are, they appear in certain instances to be closely associated with the life of the cell, for after death they cease to operate and the synthetic product is again broken down. However difficult it is to form a conception of them it may be necessary to do so, since they must form a part of any system which is put forward to explain synthesis as a result of the intervention of surface phenomena.

There is little or no doubt about the raw materials or some of the chemical reactions involved in the production of glycogen and of proteins.

Glycogen, which has the empirical formula $C_6H_{10}O_5$, has recently been shown to be constituted like starch on the basis of continuous maltose units, or, what amounts to the same thing, a conjugated chain of α-glucose units. It has also been proved that when glycogen breaks down in the liver it gives rise to glucose. Recent work suggests that there may be some configurational difference between glycogen and starch which accounts for their difference in behaviour with diastatic enzymes. Be that as it may, it appears natural to assume that the synthesis of glycogen from glucose in the cell is brought about by the simple reversal of a hydrolysis which may be catalysed by enzymes under appropriate conditions. These conditions have, however, not yet been realised in vitro.

The failure to obtain evidence of the synthesis of glycogen from the products of its hydrolysis makes it legitimate to consider whether we are right in adopting the orthodox view that the synthesis of glycogen from glucose in the living cell is brought about by a reversal of action of the enzyme or enzymes which hydrolyse it.

A consideration of all the data which have been accumulated regarding the synthesis of glycogen makes it probable that more than the mere reversal of enzyme action is concerned. It is certain that the cells in which it occurs must be supplied with oxygen. Fletcher and Hopkins also showed with muscle that its structure must be maintained and with liver the synthesis certainly only takes place in the intact organ. Do not these facts point to the conclusion that it is only the living cell that can bring about this synthesis? And if this be so, cannot we go further and suggest that the substances from which glycogen is produced or bodies derived from them must first become bound up with or at some stage form an integral part of the living structure before they are converted into glycogen. The evidence at least suggests that some such conception of the process may not be far from the truth.

Proteins.—In the early part of this century rapid advances were made in our knowledge of the structure of proteins. These advances led to a picture of protein structure which has become generally accepted—namely, that the protein molecule is formed by the union of amino-acids through an amide linkage. It is, however, unlikely that this is the only bond of union between the amino-acid units. If it were, the widely different physical and chemical properties which are met with in the proteins would have to be explained largely on the basis of their amino-acid content. The differences in composition which they exhibit do not seem to be sufficiently great to warrant this assumption. The insolubility of the keratins, for instance, although accounted for in part by the high proportion of cystin they contain, this being a very insoluble amino-acid, is possibly also due to the presence of other modes of union of the constituent amino-acids in addition to the amide linkage. Similarly, the varying degree of liability, the phenomena of denaturation, and the physicochemical behaviour of different proteins are difficult to explain solely on a basis of differences in their components. There is much still to be learnt about the actual structure of the protein molecule.

The investigation of the structure of proteins which are closely allied in origin, composition, and general chemical behaviour by immunological and in part by chemical methods has taught us how intricate the mechanism must be by which they are built up. The facts brought out by the classical work of Dakin and Dale on the albumin of the duck's and hen's egg serve to exemplify this.

The only chemical difference that could be shown between these two proteins was concerned with the disposition in the molecule of some of the leucin, aspartic acid, and histidin, which resulted in different degrees of racemisation of these amino-acids when the respective albumins were treated with caustic soda. But when used as antigens in the anaphylactic reaction they were markedly specific. These results indicate that the stereochemical structure of the molecule is different in proteins which are very similar both in general chemical properties and in biological origin. They suggest that the protein molecule produced by a particular type of cell is always built up in a distinctive and, so far as we can determine, an unvarying pattern.

We may deduce from this that although the general method of protein synthesis, that is to say, the mechanism by which amino-ac ds are joined up, may be the same in all cells, yet there must be arrangements in the cell which enable only one particular, final pattern, to result from the synthesis.

THE METHODS WHEREBY AMINO-ACIDS COMBINE.

What are the methods by which the amino-acids are caused to combine? Those used by the organic chemist in the synthesis of polypeptides can have no place in the living cell, although they have been of great assistance in helping to reveal the general structure of proteins. The use of proteolytic enzymes in an attempt to bring about synthesis under conditions which have been partially successful with other substances has often been tried and nearly as often has failed. Two examples of protein synthesis by enzyme action have been described. The most acceptable of these is Taylor's production of a protamine by a glycerol extract of clam liver from the products of its complete hydrolysis. But, so far as I am aware, this is an isolated observation which has not been extended or repeated with other protamines. The other is the preparation of so-called plasteins from the products of the partial hydrolysis of certain proteins by pepsin. A comprehensive review of the subject of plastein formation by Wasteneys and Borsook, who have themselves made notable contributions to this problem, has led them to the belief that in this phenomenon we have a true resynthesis of protein from some of the more complex of its hydrolytic products. Their work still leaves

many questions regarding protein synthesis unanswered, and not the least difficult of these is the problem of how the separate amino-acids are brought together to form the specific proteose substrates which one must postulate as combining—and in a definite order—to produce the particular protein which is characteristic of the cell which synthesises it. One of the great difficulties in accounting for the synthesis of protein by a reversal of enzyme action is that this synthesis only takes place, so far as we can observe, in a cell which is living.

The process by which the substance of the cell is increased, the building up of protoplasm, is one which must be closely allied to protein synthesis, since the material we call protoplasm is constituted for the greater part of amino-acids, united, so far as can be ascertained, by the same sort of linkage that we find in proteins. The protoplasm of the dead cell responds to all the tests by which we identify protein, it is subject to the action of hydrolytic agents in the same way, and yields identical products when hydrolysed. Ought we not therefore to look for some of the mechanisms of protein synthesis in the processes which operate when the living cell grows, and can we by any stretch of imagination account for this by a reversal of the action of one or more hydrolytic enzymes? It appears inconceivably difficult to do so. The extreme specificity of the reaction which necessitates that at a given phase of the synthesis one particular amino-acid and that one alone can be added as the next link in the molecule, requires such a multiplicity of enzymes and such a remarkable degree of control of their action as to be almost outside the range of probability. When we remember, however, that one of the prime attributes of life is that it is a dynamic condition, it does become possible to form a conception of protein synthesis in relation to that fact. The experiments of Willstätter and others have shown that to some extent the specificity of enzymes is accounted for by the "carrier" with which they are associated. It is not inconceivable that a catalyst capable of bringing about the union of amino-acids in the living cell and ultimately fashioning its protoplasm may be attached to or associated with a "carrier" which, instead of having a fixed configuration, as with the enzymes that we can extract from the dead cell, has one which is continually varying, this dynamic state being characteristic of the living material of the cell.

If, further, we could assume that the variations in the configuration of the carrier were cyclic, always going through a definite series of phases, it might be possible to account for the fact that at any particular phase of the cycle the configuration would be such as to favour the synthetic union of one particular amino-acid rather than any other because of its spatial arrangement. The assumption of cyclic changes in simple or complex living organisms is not new in physiology, and it is not unlikely that they occur in parts even of the cell itself. The phenomena of mitosis are a somewhat gross illustration of such cyclic events.

A POSSIBLE MECHANISM OF SPECIFIC PROTEIN PRODUCTION.

It is perhaps difficult to justify speculations of this kind, but it appears to me that it is at least useful as an intellectual exercise to try to arrive at some conception, founded on what little experimental evidence we at present possess, of a possible mechanism which would account for the reproduction time after time of the intricate pattern of the protein of a particular type of cell.

Whatever be the mechanism of protein synthesis there is another fact concerning it which is of interest, and that is that the cell to maintain itself must apparently contain a certain concentration of amino-acids. If these are not supplied in the animal's food then the animal supplies them by maintaining its more important tissues at the expense of others. This would suggest that the conditions for nitrogeneous equilibrium which we find in the whole animal have their replica in each cell, but the concentration of amino-acids required to maintain the equilibrium is not the same for all. Hence an amino-acid deficiency such as occurs in protein starvation leads to autolysis of some tissues before others. The equilibrium conditions appear to be set at different levels. The fact that certain amino-acids are more necessary than others in providing for this balance may be partly due to their special importance in the protoplasm of those cells which are the first to break down when protein food is withdrawn or an inadequate protein is fed.

The Site of Protein Synthesis.

The possibility that protein synthesis is associated with some part of the cell which is undergoing cyclic changes, and is thus alive, raises the interesting question of the site of this and possibly other syntheses, such as those of fat and glycogen. Are all parts of the cell—that is to say, both nucleus and protoplasm, to be regarded as alive in the sense I have indicated, and therefore to be considered as regions in which syntheses depending on life can be brought about?

It is necessary not to confuse the terms irritability and life. It is true that what we term irritability is usually taken to imply that the tissue which shows it is living, but taking the nerve-fibre as an example, it would appear that the maintenance, for a time at least, of the irritability of protoplasm and its restoration when it has disappeared—but not irreversibly—does not require the presence of the nucleus. It may require oxygen or the presence of certain ions, but this may merely mean that the labile state of the protoplasm has been upset by the products of the cell's activity, and removal of these will restore it to its irritable condition.

IRRITABILITY AND LIFE.

We have no evidence that irritability as a manifestation of what we call life is more than the possession of extremely labile structures, sensitive to minute environmental changes. The nucleus, on the other hand, is essential to the continuous life of the cell and its growth. It appears also to determine very largely the magnitude of the respiratory processes which occur in it at rest, though not necessarily the excessive respiration observed in the recovery from functional activity. Can we therefore go so far as to say that the nucleus is the seat of those synthetic activities of the cell which appear to depend on its living character rather than on its irritability, or have we to regard the protoplasm as equally living so that it is able to reproduce itself and in addition bring about such syntheses as those of fat and glycogen?

There is something to be said in favour of the idea that the protoplasm is not living in the sense in which the nucleus is, and therefore is less likely to be the seat of certain synthetic processes. It is, I think, quite a tenable view that protoplasm is made up, largely but not entirely, of combinations of amino-acids such as we find in the proteins, and that it is synthesised by the nucleus to serve special as well as certain general requirements. These special requirements must and do vary greatly with each type of cell.

Consider the mammalian erythroblast. The principal substance in its protoplasm is the protein hæmoglobin. It is doubtful whether this cell exists except to produce hæmoglobin. When it has matured the nucleus degenerates and disappears leaving the red blood corpuscle. Along with

this the respiratory activity of the cell practically disappears too, and there is not much discoverable in it except hæmoglobin. It is certainly now not living in the sense in which its progenitor, the erythroblast, was. Is it not reasonable to suggest, therefore, that the production of hæmoglobin as the erythroblast grows and matures is a function of the nucleus and not of the protoplasm of this cell? All semblance of further synthesis of hæmoglobin certainly disappears when the nucleus goes. The adoption of such a view does not imply that having produced the protoplasm of a cell the nucleus has nothing more to do with it. We know that in some indefinable way the nucleus in most cells controls the structure of the protoplasm and maintains its lability, but we have no knowledge as yet of the mechanism by which this is brought about.

In emphasising the great similarity between the growth of protoplasm and the synthesis of proteins, other examples in addition to that of hæmoglobin come to mind. The cells of the Malpighian layer of the epidermis have to produce the protein which eventually becomes the keratin of the *stratum corneum*. This would appear to be one of their chief functions. When it is done the cell dies and the nucleus becomes functionless. The production of collagen by cells of the connective tissue and of milk proteins by the cells of the mammary gland are instances of the continuous synthesis of proteins which are not labile like the protoplasm of, say, the muscle or nerve cell. Their formation, however, may be due to the operation of the same general process. They are certainly non-irritable and non-living. It is difficult to imagine that while in the cell they possess the power of reproduction but lose it once they have been cast out.

NUCLEUS OR PROTOPLASM.

If we accept the possibility that the nucleus of the cell may be the site of protein synthesis it is legitimate to consider whether the substances which appear in the protoplasm as discrete particles or masses such as glycogen or fat are produced in the nucleus or only in the protoplasm. We have no evidence as to this. The fact that they first appear as visible objects in the protoplasm is not evidence that they were produced there, and it has already been pointed out that their synthesis is apparently only possible in cells which are alive. They may be synthesised in the nucleus and stored in the protoplasm. Their disappearance from time to time may be conditioned by the liberation of enzymes from the nucleus to hydrolyse them. Such a view would do away with some of the difficulties which we experience in attempting to explain why substrates may be present in cells which, judged by their behaviour after death, appear to contain enzymes that hydrolyse them. The protoplasm, instead of producing such reserve materials, may serve as a convenient storehouse for them until the appropriate stimulus for their breakdown arrives.

One property of proteins, which may account in a general way for the presence of protein-like structure in protoplasm, is their buffering power. The nucleus is probably the most labile part of the cell. The chemical reactions proceeding in it may demand an environment that has to be finely controlled as regards changes in reaction or the concentration of certain ions. The protoplasm may thus serve as a protective layer between the nucleus and the external world, guarding it from changes which would otherwise terminate its existence. The known properties of the proteins, both chemical and physical, may be useful to this end, to which they are almost ideally suited.

Even if we can accept as possible the unorthodox view that the nucleus is the only living part of the cell, and is therefore the only part that can bring about syntheses which depend upon life, it does not solve our difficulties in explaining how they are achieved. It merely narrows down the possible sites in the cell in which they occur. The nucleus itself is a complex structure, and we have as yet few experimental methods for elucidating it. Most biologists would, I think, agree that the cell has arisen by a process of evolution from something simpler and eventually from non-living materials. It cannot have come as a "bolt from the blue." If we regard the nucleus as the only living part of the cell, then we may justly regard the protoplasm as something that has been acquired or developed in the process of evolution and is now necessary to its existence. We do not know definitely, however, of nuclear material which is living and devoid of its protoplasmic envelope unless such an arrangement is present in the bacteria. But the investigation of filtrable viruses has given an indication that material possessing the prime attribute of life—namely, the power of reproducing itself—exists, possibly in simpler forms than we find in the smallest visible organisms.

If we agree that the cell has evolved from something simpler, then we might expect to find such elementary forms of life coexisting with it did we but know how to look for them. The filtrable viruses may represent such forms, and their chemical characters may resemble those that we find in the nucleus of the cell. The ability to synthesise protein may be a property which living material only acquired at a late stage of its evolution, and that property may be one which in the process of time has come to be essential for the maintenance of the complex structure of the nucleus as we see it to-day.

DIABETES AS A PHYSIOLOGICAL PROBLEM.*

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LECTURE II.

Regulation of the Secretion of Insulin.

THE internal secretion of insulin must be adjusted from time to time according to the needs of the organism, and it is probably safe to assume that a greater secretion will be required when preformed carbohydrates, rather than protein and fat, are the foodstuffs being assimilated. When glands such as the salivary become active, definite histological changes can readily be observed in the cells, such as the extrusion into the ductules of the zymogen granules which are believed to form the precursors of the active constituents of the secretion. In the ductless glands, owing to the difficulty of exciting them to short bouts of greater activity, similar histological changes are not so readily demonstrated. Under certain conditions the isles of Langerhans, as Homans,[84] F. M. Allen,[25] and Bowie[26] have shown, show peculiar changes affecting the granules of the so-called β-cells. These conditions are fulfilled by extirpation of all the pancreas except a small graft, which may be transplanted into the abdominal wall without disturbing its blood- or nerve-supply. Because of the removal of most of the islet tissue, a great strain is put upon the remaining grafted portion to secrete sufficient insulin, and if food rich in carbohydrates be given, this strain ultimately tells on the islets, so that peculiar changes become visible in their cells, involving a hydropic degeneration of the protoplasm. There can be

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little doubt that this change is related to the insulin-secretory function of the cells, because it does not occur when the animals are treated with insulin and is much less marked if the diet does not include preformed carbohydrate. Moreover, if insulin be given to an animal in which hydropic degeneration has already started—as revealed by examination of a small portion of tissue removed from the graft—this may disappear and the cells revert to their normal condition (Allen, Bowie, loc. cit.).

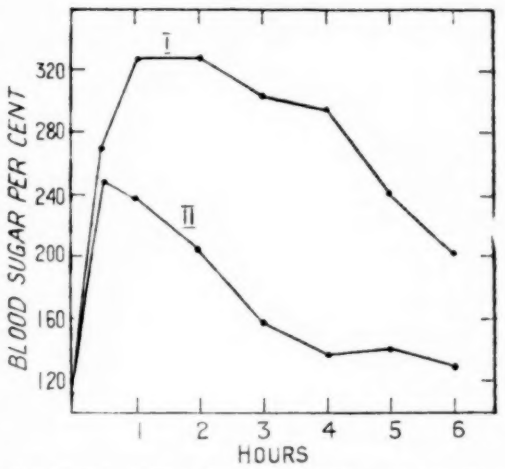
EVIDENCE THAT THE SECRETION OF INSULIN VARIES FROM TIME TO TIME.

Measurement of the changes that occur in the amount of insulin in the blood and tissues cannot be made by methods of extraction, because these are not sufficiently thorough or standardised to be carried out accurately, especially in material such as blood which contains at most only traces of insulin. The available methods for observing changes in the discharge of insulin into the venous blood of the pancreas are indirect. It is a well-established fact that the hyperglycæmia which follows upon the ingestion of sugar is much more marked in laboratory animals (rabbits) which have been deprived of food for some days previously than in recently fed ones (Bang [27]). This is well shown in the curves (Fig. 3) of experiments by Tiitso.[28] After several injections of sugar into starved animals, the hyperglycæmic response also becomes less. Similar results have also been obtained on man, especially by Staub [29] and Traugott,[30] and, as has also been shown by Thalheimer,[31] when successive small amounts of glucose are given by mouth (in man), the blood-sugar, although at first rising after each portion, finally fails to respond. If these results depend on the fact that the internal secretion of insulin is regulated by the amount of carbohydrate entering into metabolism as such, it should be possible to demonstrate that differences in the effects of insulin are dependent upon the state of the carbohydrate metabolism at the time of its injection. This has been found to be the case. For example, insulin causes the blood-sugar to fall more markedly in anmals (rats, rabbits) which up to the time when food was withdrawn before injecting them with insulin, have been kept on carbohydrate-rich food, than in animals which have been deprived of food for several days or have been on a diet poor in carbohydrate (Abderhalden and Wertheimer,[32] Tiitso [33]). Then, again, Staub [34] has made the interesting observation that transfusion into a diabetic patient of 400–500 c.cm. of blood from a healthy person who some time previously had partaken of a meal rich in carbohydrate caused the blood-sugar to fall as if insulin had been injected. When the donor had fasted for 24 hours the transfusion did not affect the blood-sugar level of the diabetic.

There are numerous other characteristics of the effects of insulin which can be adequately explained in terms of the above hypothesis. Thus, following the hyperglycæmia caused by the ingestion of sugar, the blood-sugar falls below the level at which it stood before the sugar was ingested (Folin and Berglund [35]), owing, no doubt, to the fact that the islets become stimulated by the increased concentration of sugar in the blood. There are reasons for believing that this stimulus is more effective when the sugar is absorbed from the alimentary canal than when it is given extraparentally; at least, Eadie,[36] Tiitso,[37] and I [38] were never able to observe that the blood-sugar in rabbits fell below its normal level after the hyperglycæmia caused by the intravenous or subcutaneous injection of glucose. Koref and Rigler [39] also state that the blood-sugar ultimately sinks lower in rabbits when they are injected intravenously with insulin and glucose than with the same amount of insulin alone, and corresponding results have been obtained on healthy human subjects by Depisch and Hasenöhrl.[40]

The paradoxical result is, therefore, obtained that following small doses of insulin *plus* glucose a more marked degree of hypoglycæmia becomes developed than after the same amount of insulin alone. Of course, in the former case a temporary rise in blood-sugar precedes the development of hypoglycæmia.

FIG. 3.



I. Blood-sugar curve after administration of 3 g. glucose per kg. body-weight subcutaneously in starved rabbits. Average of nine experiments. II. The same in fed rabbits. Average of ten experiments.

In all the above cases we may imagine that when there is abundance of preformed carbohydrate (free sugar and glycogen) entering the metabolism, the islets of Langerhans are stimulated to produce larger amounts of insulin than usual, and to secrete it more abundantly, in response to temporary increases in the blood-sugar.

NERVE CONTROL OF THE ISLETS.

Granted that increase in blood-sugar stimulates the islets, the question arises as to the mechanism by which it does so. We have here two distinct and separate problems: (1) does the stimulus depend on the increased sugar concentration itself, or on some related substance or on some hormone the internal secretion of which depends on the sugar? and (2), does the stimulus act directly on the islet cells or indirectly through the nervous system? In the latter case we have also to remember that the locus of action might be either the nerve centre from which the insular fibres arise or some afferent receptors acting on this centre. Let us in the first place consider the possibility of direct nerve control. In attacking such a problem, the first question that arises is the anatomical one: do nerve-fibres run directly to the insular cells, and, if so, in which nerve trunk are they carried? An apparently conclusive answer to this question has been given by various histologists. Thus, it has long been known that a rich plexus of myelinated nerve-fibres surrounds each islet, and it has been demonstrated that fine branches from this plexus invade the islets and lie between the columns of cells of which they are composed (Gentes, Pensa).[41]

Non-myelinated fibres have also been described by de Castro as penetrating the islet cells. The peri-insular plexus has been shown to be connected with branches of the right vagus nerve (McCrea and de Castro).[42]

With these facts as an anatomical basis, various attempts have been made to demonstrate that the secretion of insulin is controlled by the vagus nerve. As we have seen, there is no direct chemical method for the accurate measurement of the concentration of insulin in blood, and there is only one indirect method by which the rate of its internal secretion can be approximately gauged, that is, by observing the behaviour of the percentage of blood-sugar. If, for example, this should fall after nerve stimulation, without any other known circumstance to account for the fall, we must assume that more insulin has been secreted. The earliest attempts on record are those of de Corral,[43] working in Asher's laboratory at Berne. This worker stimulated the right vagus in anæsthetised dogs after previous section of the hepatic plexus, so as to eliminate irregularities in the rate of discharge of sugar from the glycogen of the liver. In five out of eight experiments, each lasting only a little over an hour, a small decrease in blood-sugar was observed, but the results were not conclusive.

The next attempt was made by McCormick, Miss O'Brien, and myself.[44] We used either dogs anæsthetised with ether, or decerebrate cats, and we applied electrical stimulation to the right vagus nerve as it enters the abdomen on the œsophageal end of the stomach.

In this way we avoided any interference with breathing or with blood pressure, changes in either of which may be followed by alterations in the blood-sugar level. By comparison with numerous controls, in which the nerve was not stimulated but the other experimental procedures were carried out, we succeeded very definitely in one experiment in demonstrating a prompt fall in blood-sugar during stimulation of the nerve and a more gradual return to normal when it was discontinued. In four other experiments the fall was less decided, and when the stimulation was maintained the blood-sugar either remained depressed, with some irregularities, or returned towards the normal level.

Although we did not consider these experiments as final proof that the secretion of insulin is subject to nerve control through the right vagus, there can be no doubt that they point strongly in this direction.

The problem was then taken up by Britton [45] who, using cats under barbituric acid anæsthesia, stimulated the right vagus on the œsophageal end of the stomach after cutting the branches going to this organ and to the upper intestine. As a rule, the hepatic plexus of nerves was also cut, in order to eliminate the possibility of nervous stimulation of glycogenolysis in the liver, and the left adrenal gland was removed, or its nerve-supply cut, to prevent any possible hypersecretion of epinephrine. Either of these occurrences, by causing hyperglycæmia, might mask any hypoglycæmic effect of vagus stimulation. These operations were performed several hours before the actual experiment, so that their possible disturbing effects on the blood-sugar level might have passed off. In a typical case it was found that immediately after cutting the vagus the blood-sugar rose somewhat and that it fell considerably during stimulation. This was maintained for one to three hours in the various experiments, and after removal of the stimulation the blood-sugar rose again.

The average decrease in the percentage of blood-sugar in a series of 11 experiments in which the hepatic nerves were cut was 18 mg. per hour, and in another series of 6 experiments in which they were intact it was 27 mg. The fall was greater when the level of blood-sugar was high to start with than when it was low, which is also the case when insulin is injected. Further controls were instituted to ensure, first, that the liver contained sufficient glycogen to maintain the blood-sugar level in the absence of nerve stimulation, and, secondly, that dilatation occurring in the pancreatic blood-vessels as a result of the stimulation was not in itself responsible for the hypoglycæmia by causing a more complete removal from the islets of insulin discharged at a constant rate from them. Finally, experiments were performed in which the blood-vessels and nerves of the pancreas were tied before stimulation of the vagus, which then did not affect the blood-sugar level.

The investigation was, therefore, a well-controlled one and the results show decisively that the right vagus nerve contains insulin secretory fibres. They indicate also that these have a tonic influence on the secretion. But although the presence of secretory fibres can be demonstrated under experimental conditions in which the blood-sugar is at a fairly high level before the nerve is stimulated (as in Britton's experiments), this does not necessarily mean that the islets are subject to nerve control when the blood-sugar is normal. A similar question arises in connexion with the nervous control of breathing; afferent expiratory fibres can be demonstrated in the vagus nerve under experimental conditions, but it is almost certain that these are not concerned in normal quiet breathing. Impulses to the islets through the vagus nerve may only come into play when control in other ways, such as by hormones, is inadequate to keep the blood-sugar at the normal level, or as an emergency measure.

Further investigation of the problem has, therefore, been undertaken by La Barre and his various collaborators, who have employed the methods of cross circulation between two animals which were first used in 1913 by E. Hédon [46] for demonstration of the presence of insulin in the blood. Hédon transfused the carotid blood of a normal animal into one that was depancreatised and found that this caused a decided, although not a marked, lowering of blood-sugar. By anastomosing the vein coming from the head of the pancreas of a large dog with the jugular vein of a small one (both animals being under chloralose anæsthesia), La Barre [47] obtained more striking results, no doubt because there was no dilution of the pancreatic blood by that of the rest of the body. He allowed the blood to transfuse into the smaller animal for periods of half to one hour, until its weight had increased by 100–140 g. When both animals were normal this did not cause any change in the blood-sugar level.

In a further series of observations the thorax of the donor animal was opened under artificial respiration and electrodes were placed on the right vagus nerve after it had been cut below the cardiac branches. Both adrenal glands were also removed, so as to eliminate the possibility of an increased secretion of epinephrine which might mask the effects of insulin. While the pancreatic blood of this animal was being transfused into another one its vagus nerve was stimulated electrically for a period of 15–25 minutes; after separating the animals the blood-sugar of the recipient was found to fall from about 0·115 per cent. to about 0·075 per cent.

So far the results merely corroborate those of ourselves and of Britton, in demonstrating that stimulation of the vagus may cause hypoglycæmia, but the further researches add others of far greater importance, since they show that this nerve control is stimulated by an increase in the blood-sugar.

Thus, La Barre found that the intravenous injection of glucose into the donor animal caused the blood-sugar of a previously adrenalectomised recipient to fall by about one-third and to remain at this level for three or four hours, although the transfusion of blood only lasted for half an hour. This maintained hypoglycæmia is supposed to have been due to the absence of any compensatory hyperglycæmic effect of epinephrine secretion in the recipient. The result seems clearly to indicate that excess of sugar in the systemic blood increases the insulin concentration in

the pancreatic blood, and in the next series of experiments it was shown that this depends on excitation of the islets through the vagus nerves. Thus, it was found that when these nerves were cut in the thorax of the donor or were atropinised, the injection of sugar did not lower the blood-sugar of the recipient (adrenalectomised) dog.

Under the same experimental conditions injection of epinephrin into the donor also caused hypoglycæmia in the recipient, but in this case previous vagotomy did not abolish the hypoglycæmic effect in the donor (Zunz and La Barre), indicating that epinephrine has a direct stimulating action on the islets. When insulin hypoglycæmia was induced in a donor upon which adrenalectomy had been performed, transfusion of its blood into a depancreatised dog did not lower the blood-sugar level. This result shows that the secretion of insulin is suppressed by hypoglycæmia, since, as we have seen, the pancreatic vein blood of a normal animal lowers the blood-sugar of a depancreatised recipient.

That it is on the centre of the vagus and not on its efferent pathway that the hyperglycæmic blood acts was shown by an experiment in which three dogs were used.

Between two of them (A and B) a double carotid jugular anastomosis was established and the remaining blood-vessels in the neck of B were ligatured. In this way the brain of B was perfused by the blood of A. The vagus nerves of B were left intact and the body of the animal was kept alive by artificial respiration. The pancreatic vein of B was then anastomosed with the jugular of the third dog, C, and it was found that injection of glucose into A caused the blood-sugar of C to fall and to continue depressed for several hours after the animal was separated from B.

The results of these amazing experiments would appear to demonstrate beyond all doubt that the secretory activity of the islets is under control of the vagus centre, and that this is stimulated by an increased concentration of glucose in the blood. This nerve-control is of importance in connexion with glycogen formation in the muscles. Thus, after glycogen has been removed from the muscles of a spinal cat by stimulating them, it will not reappear unless excess of insulin is injected. On the other hand, it will reappear in an anæsthetised cat with brain intact without injecting insulin, but will fail to do so if the vagus nerves are cut (especially the left one), or if the pancreas is removed (Debois and Hoet [48]).

The exact relationship of the vagus to the secretion of insulin is, however, not yet quite clear. G. A. Clark,[49] for example, has adduced evidence to show that, as well as exciting, this nerve may inhibit the secretion of insulin. He found in rabbits that drugs which stimulate the parasympathetic system cause a lowering of blood-sugar, but usually fail to do so after section of the right vagus. Clark points out, however, that vagal control of insulin secretion can only come into play under certain circumstances and cannot be essential for maintaining the blood-sugar level, at least in animals leading a placid life in confinement. Thus, shortly after section of the right vagus below the cardiac branches in rabbits the blood-sugar fell immediately, and there was no indication of decreased tolerance following the intravenous injection of glucose (1 g. per kg.). On the contrary, the blood-sugar curve returned more rapidly to normal, thus suggesting that the injected sugar was being better dealt with than it had been in the same animal before vagotomy. After a period of two months, however, the condition became reversed and the hyperglycæmia following the injection of glucose lasted decidedly longer than usual. The insulin-regulatory fibres in the right vagus would appear from these results to be of two kinds, tonic inhibitory and secretory; but even if we adopt this hypothesis to explain Clark's results we are left with the problem, why the tolerance for sugar should be actually depressed in two months after the vagotomy (Clark).[50] It may seem strange that through the self-same nerve there should come to the islets impulses which may either stimulate or inhibit the internal secretion of insulin, but it must be remembered that much the same state of affairs exists in the afferent impulses to the respiratory centre. In view of the results of these various experiments there can be little doubt that the vagus centre exercises some sort of control over the internal secretion of insulin, but it is difficult to estimate its physiological significance.

HORMONE CONTROL OF THE ISLETS.

That nerve control comes into play under certain experimental conditions does not necessarily mean that the variations which occur in the discharge of insulin into the blood under the ordinary conditions of life are regulated in this way. Indeed, on a priori grounds it seems more probable that the islets are under chemical rather than nerve control. Nerve control of glands is highly developed when these have to secrete promptly, as is the case with the salivary, the lacrymal, and the sweat glands, but hormone control becomes predominant when the secretion is only required gradually, as that of insulin must be. Assuming, then, that the islets are also affected by chemical substances in the blood, the question arises as to the nature of the latter. Changes in the concentration of sugar in the blood may act directly on the islets, or a hormone derived from some other ductless gland, the secretion of which is regulated by the state of the blood-sugar, may be responsible. It is possible, for example, that whenever the tension of glucose tends to rise above a certain level some other ductless gland is stimulated to secrete a hormone, which then acts on the islets so as to bring about the secretion of insulin. Speculative hypotheses of this type have from time to time been freely put forward in connexion with carbohydrate metabolism, but there has been little direct evidence to support them, no more indeed than the fact that changes in the blood-sugar level, or in the tolerance for carbohydrate, can be brought about by removing some gland, or by injecting extracts of it. When we bear in mind the extreme complexity of the factors which control carbohydrate metabolism it is evident that such hypotheses are of little value and can serve to stimulate further inquiry provided only that they are based on some firmly established facts.

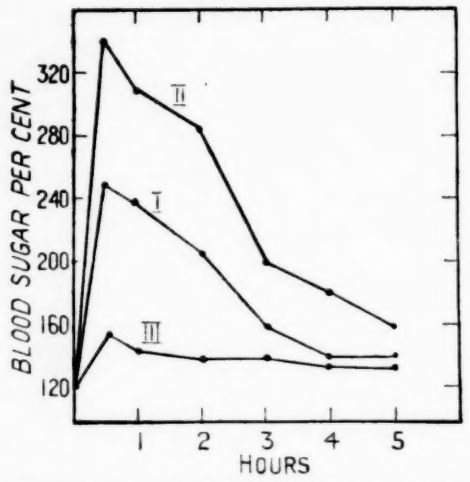
Are there, then, any facts which show that other hormones than insulin have an influence on carbohydrate metabolism and, if so, do they act directly on the various mechanisms concerned in the production or utilisation of sugar, or indirectly by influencing the secretion of insulin from the islets? I will take by way of example the results which have been obtained by various investigators who have experimented with the thyroid gland.

It has been known for some time that the assimilation limit for sugar is significantly altered by thyroidectomy, or by feeding with thyroid (Cramer and Krause,[51] Kuriyama [52]), and that the susceptibility of sheep towards insulin can be made to change by similar treatment (Bodansky [53]). But the results which I wish more particularly to discuss are those obtained by Burn and Marks,[54] who showed that after thyroid gland had been daily added to the food of rabbits for about a week the animals became relatively insensitive towards insulin, so that hypoglycæmic symptoms did not supervene even when they were injected with ten times the usual convulsive dose. At this stage it was also found that the injection of epinephrine resulted in a much greater increase in blood-sugar than usual. These results could most simply be explained as being due to a rapid breakdown of hepatic glycogen, but since this substance was found by actual analysis to be unchanged in amount, it was concluded that its stability had become diminished, so that it was more readily discharged as sugar

into the blood in response to the stimulus, either of a lowered blood-sugar level or of the presence of excess of epinephrine.

After the thyroid feeding had been kept up for two or three weeks, a complete reversal occurred in the response of the animals to insulin and epinephrine; they became hypersensitive to the former and irresponsive to the latter hormone. Confirmatory results were obtained by comparing the extent to which administration of sugar produced hyperglycæmia at various stages of thyroid feeding. For example, in the curves of Fig. 4, which are taken from the work by Tiitso in my laboratory and in which the extent of the rise in blood-sugar is compared in normal rabbits (I.), with that occurring in the same animals after feeding for a week (II.), and for longer periods (III.), with thyroid, there is at first an increase and then a marked decrease in the hyperglycæmic response to sugar. After prolonged thyroid feeding, therefore, the animal becomes extremely sensitive towards insulin injections, whereas epinephrine can scarcely

FIG. 4.



I. Blood-sugar curve following subcutaneous injection in normally fed rabbits. II. The same in rabbits fed for five to six days with thyroid. III. The same in rabbits fed for more than ten days with thyroid.

cause hyperglycæmia, and administration of sugar either fails to affect the blood-sugar level—as in Tiitso's observations—or, as Marks has shown, may actually cause the blood-sugar, after a slight preliminary rise, to fall to the level at which fatal hypoglycæmic symptoms supervene.

How are these results to be explained? The prolonged thyroid feeding is associated with a practical disappearance of glycogen from the liver, but, although this might in itself be considered as adequate to explain the results with insulin and epinephrine, it fails to account for the intense hypoglycæmia which follows sugar administration. There is some probability that Marks's explanation is the correct one—namely, that the administration of sugar causes increased secretion of insulin from the islets. Prolonged administration of thyroid seems, therefore, to bring about two definite changes in carbohydrate metabolism: it renders the liver incapable of forming—or at least of storing—glycogen, and at the same time it greatly sensitises the secretion of insulin. The upset of the glycogenic function is undoubtedly secondary to the excessive secretion of insulin, for, although both Goldblatt [55] and Sahyun and Luck [56] have shown that glycogen accumulates in the liver at early stages after the injection of this hormone in young rabbits, there is abundant evidence to show that its effect is to depress it in other animals.

I have chosen these results as offering the best evidence I know in support of the view that the secretory function of the islets is subject to control by hormones derived from other glands, but even they are not entirely convincing, for we have to bear in mind that thyroxin also has a profound effect on metabolism in general. Its calorigenic effect, for example, indicates that it alters the metabolic rate of the tissues, and it is permissible to suppose that the influence which it has on alimentary hyperglycæmia is dependent upon its causing over-stimula tion of the assimilatory powers of the tissues. We can see, therefore, that the answer to our main question, whether changes in the glucose concentration of the blood affects the islets directly or indirectly—either through hormones from other glands or by nervous control—cannot as yet be expected to be a final one.

Ætiological Factors Involved in Human Diabetes.

In the light of these experimental results, it may be of interest to examine in a general way the ætiological factors which are believed to be involved in human diabetes. Disregarding entirely the inherited tendency to the disease and its possible occurrence as a result of luetic or other infective lesions involving the islets, it may be stated that there are three conditions which seem clearly to lead to its development—over-eating, obesity, and nerve strain. It seems to be accepted by physicians that intemperance in eating, especially when coupled with sedentary habits, is decidedly predisposing to diabetes, and it is at least possible that this may depend on a continued overstraining of the islets. We can imagine that the continued call for insulin when carbohydrate metabolism is working under high pressure leads to a breakdown of the overworked insular cells, a view which has been supported by F. M. Allen's experiments on partially depancreatised dogs. Granted, then, that intemperance in diet may lead to a breakdown in the insulin-producing function of the islets, the question arises whether the over-stimulation of their cells occurs through their nerve control or through direct action of some hormone on them. It appears to me to be most unlikely that the former could be the mechanism involved, since no condition is known in which persistent over-stimulation of nerve-supply brings about degeneration or atrophy of the organ or tissue concerned. It is much more likely that a humoral mechanism is involved. On the other hand, it seems that it must be through a breakdown of the nerve control that the islets come to function inadequately in those cases in which the incidence of diabetes is related to conditions of nerve strain. But it will require much further analysis of this relationship to make it certain that these supposed nervous cases do not really belong to the dietetic group. An analysis in this direction by Joslin has made it at least not impossible that most of the cases in which the chief ætiological factor has appeared to be a nervous one can be shown to have been in patients who were assimilating food beyond their metabolic requirements.

Methods for Detecting Changes in Insulin Secretion in Man.

Intimate association between the experimentalist and the clinician has been a feature of research in carbohydrate metabolism. Much of the information revealed by experiments on animals has been an invaluable guide in the control of diabetes in man and, on the other hand, careful observation of this disease by the clinician has frequently indicated to the experimentalist the pathway along which he should proceed in searching further for the nature of

the metabolic fault which causes it. Without the mutual coöperation of the two groups, it is certain that we should not now be in possession of a means by which the diabetic can be relieved of all his symptoms, so that he can follow his usual pursuits with but little, if any, handicap.

One of the most interesting of the problems which lie on the border-line between laboratory and clinic concerns the control of the secretion of insulin in man; whether this undergoes alterations under normal conditions and whether such alterations, if they occur, have any relation to the onset of diabetes. The symptoms by which an increased internal secretion of insulin may be recognised in man are: (1) actual hypoglycæmia while in the basal state; (2) an excessive fall below the normal level of blood-sugar following post-prandial hyperglycæmia; and (3) an excessive difference between the sugar percentages in capillary and venous blood. Spontaneous (idiopathic) hypoglycæmia in man may be suspected when the basal blood-sugar is found to be lower than 0·08 per cent. Sometimes it may fall well below the usual convulsive level without the development of any definite symptoms, cases having been reported in children in which the percentage of blood-sugar was only 0·038 without anything abnormal being observed in their behaviour (Talbot, Shaw, and Moriarty [57]). Even when hypoglycæmia is present it cannot be regarded as a certain sign of hyperinsulinism, since the blood-sugar may fall far below its usual level in perfectly normal conditions, as after strenuous and prolonged muscular exercise. Here the rapid utilisation of the glycogen of the muscles must be regarded as the primary cause of the hypoglycæmia, and it is of interest that the ingestion of sugar usually gives prompt relief to many of the subjective symptoms of fatigue. The blood-sugar may also fall to an unusually low level when milk is being actively secreted both in the depancreatised dog and in the milch cow, but Harding and Downs [58] deny that it becomes subnormal in nursing women. With these reservations, however, we are probably correct in regarding as indicative of hyperinsulinæmia any condition in which the basal blood-sugar is persistently below the limits which I have indicated.

It is possible that the second and third methods to which I have referred are capable of detecting alterations in the secretion of insulin in man that would not appreciably affect the basal blood-sugar level, and Depisch and Hasenöhrl [59] have paid attention to this problem. They consider that the blood-sugar should not fall by more than 20 per cent. below the normal level after the hyperglycæmia caused by 100 g. of glucose, and that the differences between the percentages of sugar in venous and capillary blood in about one hour after beginning to drink the sugar solution (10 per cent. taken slowly during half an hour) should not exceed about 15 per cent. The principles upon which these methods depend have been established by the work of numerous investigators, both experimental and clinical, more especially by Frank, Nothmann, and Wagner.[60] It is claimed for them that they tell us directly whether or not insulin is present in proper amount, and not merely whether the abnormal reaction to sugar depends on a balanced effect of insulin and other hormones acting on the glycogenic function of the liver. According to Depisch and Hasenöhrl, deviations from the "normal" difference can be detected in non-diabetic persons in whom there is a tendency to obesity or to excessive leanness. In diabetes itself the difference disappears. It will take considerable investigation to ascertain whether these methods are really any more dependable than that of the sugar assimilation curve for detecting early stages of diabetes or other pathological disturbances of carbohydrate metabolism.

Hyperinsulinism.

What more particularly interests us is a consideration of the cases in which hyperinsulinism becomes of clinical significance. Although earlier cases have been reported that of Wilder, Allan, Power, and Robertson [61] is the most complete.

Their patient was a surgeon, aged 40, who, in November, 1925, after an unusually long day in the operation theatre, was overtaken by weariness, confusion, and ultimately by collapse, these symptoms being promptly removed by taking an egg-nog. Attributing his condition to hyperinsulinism, the patient found that he could ward off attacks by taking food at frequent intervals. As time passed the tendency to hypoglycæmic symptoms increased and it became necessary for his wife to watch for signs of unusual behaviour while he was asleep, and to give him sugar for their relief. Some time before the onset of these symptoms those of gastric distress and of renal colic had been experienced, and at one time mild diabetes had been diagnosed. In October, 1926, when the patient came under the care of Wilder and his associates, it was found that the symptoms manifested themselves in a little over three hours after the noon-day meal, when the blood-sugar was 0·055 per cent. In four hours they became pronounced, and included perspiration, muscular twitching, and incoherence of speech. The blood-sugar at this stage was 0·036 per cent., and 15 minutes later, when it was 0·027 per cent., the development of stupor and convulsive jerkings made it necessary to give sugar, with the result that in ten minutes recovery was well established. From among the other clinical data, the following are of significance: 1. Administration of either epinephrin or pituitrin did not affect the hypoglycæmic symptoms or delay the fall in blood-sugar. 2. When sugar solution was continuously delivered into the duodenum through a tube, from 20 to 25 g. an hour were required to ward off the symptoms.

On Dec. 4th an abdominal operation revealed a cystic tumour in the tail of the pancreas and a hard nodular one in the right lobe of the liver. A small portion of the normal liver substance was removed and found to contain 3·49 per cent. of glycogen. This is of great physiological importance, since it indicates that the failure of epinephrin to combat the symptoms was not due to an insufficiency of hepatic glycogen, from which this hormone might produce sugar. The post-operative management of the case was difficult and demanded the continuous intravenous injection of glucose for 63 hours, when the nausea disappeared and glucose could be given by mouth. The condition became worse after the operation, so that the daily glucose value of food (sugar *plus* other food) had to be increased to 1000 g. to ward off the hypoglycæmic symptoms. The patient died one month after the operation.

Examination of the tumours removed, within three hours after death, from the pancreas and the liver showed the former to consist of focal masses of tumour cells embedded in a dense connective tissue stroma and arranged in irregular strands and islands. The cells had a striking resemblance to those of the isles of Langerhans, and here and there some of them were degenerating. But the most significant observation was that the neoplasm in the liver was also composed of similar cells. It was identified as a carcinomatous metastasis arising from the island cells, and an extract made from this metastasis showed it to contain a relatively large amount of insulin. Neighbouring portions of healthy liver similarly extracted were found to contain no insulin, but to be loaded with glycogen (8·25 per cent.).

This excellently described case establishes the existence of a hitherto unknown disease, and since its publication others have been described by McClenahan and Morris,[62] by Thalheimer and Murphy,[63] by F. N. Allan,[64] and by Howland, Campbell, Maltby, and Robinson.[65] These are important because they carry us a step further in showing that the hypoglycæmic symptoms may be cured by surgical operation.

Allan's patient, a farmer 52 years of age, had suffered frequently, for about two years before he came under observation, from attacks of weakness and stupor which could at first be warded off by taking food at short intervals. At the time the patient came under observation the blood-

sugar while fasting fell to 0·04 per cent., at which level the usual hypoglycæmic symptoms supervened and, since these could no longer be satisfactorily controlled by taking food, it was decided to operate. No tumour being found in the pancreas, a portion (14 g.) was removed so as to restrict the production of insulin. This apparently resulted, since the hypoglycæmic attacks became much less frequent, three meals a day being as a rule adequate to prevent them.

The case described by Howland et al was a woman, aged 52, in whom convulsions and coma, along with mental symptoms and excessive sweating, had been frequent for six years before admission to hospital. Hypoglycæmia was found, but the most remarkable feature of the case was the erratic response to carbohydrate administration (dysinsulinism). Thus, intravenous injection of glucose solution would remove the coma only temporarily, whereas, when sugar was given by mouth, recovery was satisfactorily maintained and the blood-sugar rose to diabetic levels. Operation was decided upon, and a pancreatic tumour was found, which proved to be a slowly growing carcinoma. It was removed, with the result that the patient—during the 14 weeks which the record covers—remained free from her previous symptoms.

These case-histories are invaluable ready-made experiments, which demonstrate that the islet tissue may proliferate and become hyperactive during adult life. In Allan's case the proliferation was unaccompanied by tumour formation, and this would seem to me to indicate the possibility that excessive variations in insular activity may sometimes be a cause of vague metabolic disturbances in man, particularly of those in which either abnormal corpulence or leanness is the chief symptom. Various clinical observers have had this possibility in mind (cf. Falta [66]), and I would venture to suggest that it should continue to be examined by such methods as I have outlined.

That the islet tissue may vary in amount from time to time opens the question of its derivation, and it is interesting to recall the oft-repeated conclusion of Laguesse [67] that the duct epithelium is not the only structure from which insular cells may be derived, but that the acinar cells may also become transformed into them.

Hypoglycæmia in Diabetes.

The hypoglycæmia we have just been considering differs essentially from that which is not uncommonly met with in diabetic patients. The main cause of the greater susceptibility of the diabetic to insulin is inadequate storage of glycogen in the liver, for although this substance may continue to be formed out of protein and fat, it cannot be stored up sufficiently in the liver to meet the extra demands of the organism for sugar (cf. Joslin [12]) occasioned either by excess of insulin or by increased muscular activity. Muscular fatigue is therefore to be avoided in diabetic patients, although graded exercise is beneficial in that it reduces the requirements for insulin (cf. Gerl and Hofmann [68]). When the demands of the organism for sugar become excessive, as after sustained muscular effort, hypoglycæmia of sufficient degree to cause marked symptoms may supervene even in perfectly normal persons (marathon runners) and the symptoms can be immediately relieved by the ingestion of sugar (Levine, Gordon, and Derick [69]). In epilepsy in children and in progressive muscular dystrophy hypoglycæmia is also said to occur.

Substitutes for Insulin.

The activity of the islets can probably be stimulated by various drugs acting on them either directly or through the nervous system. From a therapeutic standpoint this is of very great importance, since it is obvious that relief could in this way be obtained from the diabetic symptoms but at the risk of causing a further deterioration of the secretory powers of the already overtaxed islet tissue. Among the substances which may act in this way, synthalin, myrtillin, and bile-salts deserve some attention, the first two more especially as having been recommended as substitutes for insulin in the treatment of diabetes. Since whatever effects they may have are manifested when they are given by mouth, much attention has been devoted to seeing whether they really possess any clinical value and might therefore be used in cases in which hypodermic medication is undesirable.

Synthalin is a compound containing two molecules of guanidin along with ten or more of methylene (dodekamethylendiguanidin). It was introduced by Frank, Nothmann, and Wagner,[70] who showed that although guanidin itself lowers the blood-sugar in rabbits, as had previously been known, it does not significantly do so in depancreatised dogs, whereas synthalin acts on both. The hypoglycæmia which synthalin produces is often preceded by hyperglycæmia, this depending on dosage, and also—according to Bodo and Marks [71]—on the glycogen content of the liver. These workers also found that synthalin lowers the sugar in the fluid perfused through the isolated muscles of the leg (in dogs), and raises the respiratory quotient of eviscerated spinal cats. But these results may not be of much significance, since lactic acid also accumulates in the blood. Synthalin inhibits the deposition of glycogen in the liver of rabbits after ingestion of sugar (Rubino, Varela, and Collazo [72]) and causes damage to the liver cells, especially on repeated administration (Hornung [73]), Fuentes,[74] Simola [75]). Although Frank, Nothmann, and Wagner [76] state that synthalin in its latest form and in suitable dosage is effective in lowering the blood-sugar and in alleviating the other symptoms of diabetes in depancreatised dogs without causing any liver damage, this has not been the experience of others (Rathery, Kowiilsky, and Gibert [77]), and it therefore signifies but little that the drug may temporarily revive fasting phlorhidzinised dogs that are comatose from acidosis. If it has any effect in diminishing the diabetic symptoms in phlorhidzin poisoning, this can easily be attributed to its stimulating action on the internal secretion of insulin. In face of all these experimental results it is not surprising that synthalin should have proved to be an unsuitable, if not indeed a dangerous, drug to use in the treatment of diabetes in man (Graham and Linder,[78] and Joslin [79]).

It is possible, as Bischoff, Sahyun, and Long [80] have shown, that guanidin compounds having insulin-like effects on normal animals even more pronounced than those of neosynthalin may be discovered, but I do not consider that any of them should be used in the treatment of diabetes in man until it is definitely established, not only that they can remove all the symptoms of this disease in completely depancreatised dogs, but also that they can keep the animals in perfect health for a period which is, at least, much longer than that which Soskin has shown is possible in the case of untreated animals.

What I have said of synthalin applies also to myrtillin, although this drug has the advantage that it does not apparently have a toxic action on the liver. It is, at least, harmless. Myrtillin was prepared by F. M. Allen [81] from the leaves of plants of the myrtle family, it being believed among the Alpine peasantry that infusions of these leaves have antidiabetic properties. Myrtillin has been said to relieve the symptoms of diabetes in partially depancreatised dogs and to prolong their lives, but it has no effect on the blood-sugar level in normal animals, nor does it in the slightest degree influence the

symptoms or the course of the diabetes in completely depancreatised dogs, as was shown in my laboratory at Toronto by Drs. Chaikoff and Soskin. In the light of these laboratory findings I can see no justification for attempting to use myrtillin in the treatment of diabetes in man.

The results of bile-salts are not very striking. Horsters [82] has shown that 1 g. orally, or 0·5 g. intravenously (especially denoxycholalic acid), after withholding food for 24 hours, may lower the blood-sugar in rabbits to about 50 per cent. of the normal. Similar results were obtained in dogs, in which the stimulating effects of these salts on the pancreatic secretion were also readily demonstrable. On the other hand, no hypoglycæmic effects were obtained by giving bile-salts to diabetic (depancreatised) dogs, so that their action is clearly dependent upon stimulation of the secretion of insulin by the islets. It is suggestive that both the internal and the external secretions of the pancreas should be stimulated in this way, and there is some evidence that the pancreatic secretion in man is increased after insulin injections.[83]

The researches which I have just reviewed do not encourage the hope that some substitute for insulin, capable of acting by the parenteral pathway, will be discovered, nor does it appear likely that any means will be found by which insulin itself can be made to display its action by other methods of administration than injection subcutaneously or intravenously. Murlin and Hawley,[84] and Miller,[85] have given much attention to the possibility that the ingestion, either of very large amounts of insulin itself or of insulin dissolved in alcohol and contained in keratinised capsules, might be efficacious, but the results are not sufficiently positive to justify the risk of attempting such methods in the clinical treatment of diabetes. The difficulty is, of course, that insulin is rapidly destroyed by the digestive ferments. This suggests its close relationship to protein, and it is significant that crystalline insulin, as prepared by Abel [86] and his pupils and by Harington and Scott,[87] possesses many of the characteristics of protein. By hydrolysis of crystalline insulin various amino-acids have been isolated (arginine, histidine, and leucine) and sulphur is present in relatively loose combination, but it is not yet certain whether the antidiabetic properties are dependent upon the molecule as a whole or on some side group—for example, that in which the sulphur is contained. It is at least significant in this connexion that four different samples of crystalline insulin, two of them prepared by Abel's method and two by that of Harington and Scott, should have been found to possess practically the same strength, 23·3 units per mg., when assayed—by comparison with the international standard preparation—on both rabbits and mice. Since this value is also reached by the best commercial preparations of insulin, which are amorphous, it does not appear that crystalline preparations do much to reveal the nature of insulin. Insulin appears to be as intangible as vitamins and enzymes; like these, its activities may depend on some little-understood molecular grouping which, by contact rather than by actual combination, renders the glucose molecule unstable so that it can more readily be utilised in metabolism. Carr, Culhane, Fuller, and Underhill [88] recently obtained significant results showing that insulin can be completely inactivated by treatment with ethyl alcohol and hydrochloric acid; the reaction is a reversible one, since the original potency can be completely restored by treatment with dilute sodium hydroxide. It is suggested that the change undergone by insulin by this treatment is an esterification but, whatever may be its nature, the fact that reversible inactivation occurs opens up interesting possibilities with regard to the behaviour of insulin in the body.

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LUNG PUNCTURE IN ACUTE LOBAR PNEUMONIA.

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Exploratory puncture of the pleural cavity has been employed as an aid to clinical diagnosis for many years, and its value has been well established. Exploratory puncture of the lung substance, on the other hand, has been used but seldom, and its value as a clinical procedure has neither been generally advocated nor established. In 1909, Horder [1] described lung puncture as "a new application of clinical pathology," and showed that in cases of pneumonia, of abscess of the lung, and of bronchiectasis lung puncture could be of the greatest assistance in arriving at a diagnosis. In 1920, Thomas and Parker [2] studied the results of "ante-mortem" lung puncture in an attempt to throw some light on the mechanism of crisis in lobar pneumonia, and showed that the death of the pneumococcus was not the factor which causes or initiates crisis. These results do not concern us at the moment; the point of interest about their work and that of others [3] is that lung puncture was performed in a large number of cases, often many times in the same patient, without any evidence to show that it was either a hazardous procedure or associated with any serious complication.

In the Royal Infirmary, Edinburgh, during the past winter, a number of cases of acute lobar pneumonia have been treated with an antiserum for Types I. and II. pneumococcus. As this serum was expensive and difficult to obtain in large amount, it was essential that its use should be strictly limited, if possible, to cases of infection by these types. Accordingly, an attempt was made to ascertain the type of organism at the earliest opportunity. By the usual means of determining the serological type of pneumococcus in sputum,[4] the necessary information on this point was obtained within 6 to 18 hours after the patient's admission; but in a certain number of cases—most frequently those admitted at an early stage in their illness—no sputum could be obtained for several days, and occasionally not until actually after the crisis. By puncture of the lung substance over the affected lobe it was found that in the majority of such cases a pure culture of pneumococcus could be obtained.

TECHNIQUE OF LUNG PUNCTURE.

The method of puncturing the lung substance is similar to that of pleural puncture. In both cases the site of puncture is determined to a great extent by the physical signs. Generally speaking, where the signs indicate exudate or consolidation, there are chances of obtaining a culture of the organism by puncture over that area. In the clinical examination of 74 patients with acute lobar pneumonia during the past six months, it was noted that lower lobe lesions were present in approximately 90 per cent. of the cases. In each patient on whom lung puncture was performed by the writer, one or other lower lobe was apparently affected at the time of puncture, and the lung substance was entered through the seventh, eighth, or ninth intercostal space posteriorly in the mid-scapular line.

The needle is an ordinary exploratory needle of rather fine bore, about 10 cm. in length, attached to a 20 c.cm. Record syringe with a well-fitting piston. The skin is cleansed in the ordinary way, and local anæsthesia with 2 per cent. novocain is induced at the selected site. The needle is then inserted directly into the lung substance for 8 to 10 cm., and the piston slowly pulled back. As the result of suction one or two drops of blood-stained fluid may occasionally enter the syringe. The needle is now gradually withdrawn and, as the pressure becomes lower, some drops of fluid spurt into the barrel of the syringe. This fluid, which may amount only to one or two drops in the needle, is then mixed with 5 c.cm. of phosphate broth (pH 7·6–7·8), 1 c.cm. of this mixture being immediately injected into the peritoneal cavity of a mouse and the type of organism determined in the usual way.

RESULTS IN PRESENT SERIES.

Lung puncture was performed in 17 cases of acute lobar pneumonia. It was primarily done in patients who had at the time no sputum from which the type of the infecting organism could be determined.

Table I.

Case.	Day of illness on day of admission.	Lung puncture fluid type.	Day of admission when puncture performed.	Sputum type.	Day of illness when sputum obtainable.
1	2	I.	2	—	—
2	2	I.	1	I.	4
3	4	—	1	II.	6–7
4	3	I.	1	—	—
5	2	—	1	—	—
6	3	II.	2	II.	4
7	4	I.	2	—	—

Table I. shows a group of seven cases which had no sputum at the time of admission. In five of these a positive culture of pneumococcus was obtained from lung puncture. Two cases yielded no growth of pneumococcus, either by mouse inoculation or by direct culture. Sputum was available at a later date from one of these cases; the other patient had no sputum at any time during the course of his illness, and in that case, therefore, the type of pneumococcus was not determined. Of the seven cases three eventually had sputum, and the type of pneumococcus present was found to be the same as that demonstrated by lung puncture. In four cases no sputum was obtained at any time during the course of the illness, and in these cases the type of pneumococcus was determined from lung puncture alone.

Table II.

Case.	Day of illness on day of admission.	Type of pneumococcus. Sputum.	Type of pneumococcus. Lung puncture fluid.	Case.	Day of illness on day of admission.	Type of pneumococcus. Sputum.	Type of pneumococcus. Lung puncture fluid.
8	3	II.	II.	12	6	IV.	—
9	5	I.	I.	13	4	II.	II.
10	5	I.	I.	14	2	I.	—
11	3	II.	II.	15	3	II.	II.

Table II. represents a group of eight cases where sputum was obtainable from the beginning of the illness. Lung puncture was performed to confirm if possible the type of pneumococcus found in the sputum, and in six of the cases the same pneumococcus was isolated by inoculation of a mouse. In the two negative cases no growth of pneumococcus or other organism was obtained from lung puncture; in one case the puncture was completely "dry," but in the other some blood-stained fluid was present in the syringe after puncture.

Case 16 (Table III.), a youth of 23, was admitted on the third day of his illness. From sputum, blood, and lung

puncture fluid a Type II. pneumococcus was obtained. The patient died three days later, and post mortem lung culture also showed a Type II. pneumococcus.

TABLE III.—*Results of Bacteriological Examination of Two Fatal Cases.*

Case.	Day of illness on day of admission.	Type of pneumococcus.			
		Sputum.	Lung puncture fluid (ante-mortem).	Blood culture.	Lung culture (post mortem).
16	3	II.	II.	II.	II.
17	5	I.	I.	I.	I.

Case 17, a woman of 48 years, was admitted on the fifth day of her illness. Similarly, from sputum, blood, and lung puncture, a Type I. pneumococcus was obtained, and at post mortem a Type I. organism was found on lung culture.

A pneumococcus was isolated from the "lung fluid" of 13 out of 17 cases. In each case, in addition to the animal inoculation method, the lung fluid was cultured on blood-agar. In four cases there was no growth; in eight cases a pure culture of pneumococcus was obtained; and in five cases a culture of pneumococcus was found, with an additional growth of staphylococcus. In the four cases where no growth was obtained lung puncture was performed on the first day of admission. The physical signs at that time were not a definite indication of the location of the disease, as is often the case in the first two or three days of a deep-seated pneumonia, and the only clue to the site of the pneumonia in three of the cases was the presence of pain over a particular area of lung. No further puncture was performed in any of these four cases. It may be concluded, therefore, that in these cases the site of puncture did not coincide with a focus in the lung where living pneumococci were present in sufficient numbers to be demonstrated by cultural methods.

The question has arisen from time to time whether the strain of pneumococcus isolated from sputum is identical with the strain responsible for the actual pulmonary lesion, particularly when the sputum strain is a Type IV.—that is, a type which so often occurs as a commensal in the throat. It is only on the rarest occasions that a Type I., II., or III. pneumococcus can be demonstrated in the lung lesion post mortem when during life the only pneumococcus isolated from repeated examinations of the sputum has been a Type IV. The results, therefore, are of interest in showing how the type isolated directly from the lung during life corresponds to that found in the sputum. In the two cases noted in Table III. the pneumococcus isolated from the sputum, lung fluid, and blood during life was found to be similar in type to that demonstrated in the lung substance post mortem, again showing that the type of pneumococcus found in the sputum in acute lobar pneumonia is most probably the same as that causing the lesion.

POSSIBLE DANGERS.

After Horder's description of the procedure in 1909 a certain amount of criticism was evoked, mainly on the ground that the procedure was dangerous. THE LANCET suggested in an editorial[5] that "the occurrence of hæmorrhage from wounding a vessel or an aneurysm of the pulmonary artery" was a disadvantage which had to be taken into account. But even if a vessel of moderate size were punctured by a fine-pointed needle the resultant hæmorrhage would probably be of little clinical or pathological significance. Aneurysm of the pulmonary artery, too, must be of the greatest rarity. In septic pneumonia, infection of a healthy pleura might be a possibility, but in pneumococcus pneumonia it is difficult to see how any further infection of the pleura could possibly occur by its transitory puncture with a well-sterilised and fine-pointed needle. Sudden death caused by reflex inhibition of the cardiac and respiratory centres, due to irritation of the afferent fibres of the vagus, has also been suggested as a real though somewhat rare and uncommon danger.[6] It is improbable, also, that a condition of artificial pneumothorax could be induced, particularly if a fine needle is used, attached to a syringe with a well-fitting piston.

In the present series of cases no complication, direct or indirect, was noticed as a result of lung puncture. At the time of puncture no phenomenon such as increased dyspnœa, troublesome cough, or marked increase in the pulse and respiration-rate was noted. In almost every case pain, either at the time of puncture or after, was negligible. Occasionally short stabbing pain was experienced when the needle penetrated an inflamed and over-irritable pleura, but it was only momentary and of no marked clinical significance. Owing to the fact that puncture was usually performed in a patient too ill to realise exactly what was happening, the psychological factor of expectancy was, in the majority of cases, absent.

CONCLUSIONS.

In cases of acute lobar pneumonia without sputum, or with very little sputum, where for therapeutic reasons it is desirable to know the type of organism as soon as possible, lung puncture may be of value, and in some cases may be the only way to ascertain what type of pneumococcus is present.

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GLANDULAR FEVER.

AN EXPERIMENTAL INVESTIGATION.

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RATHER towards the end of the epidemic of glandular fever that occurred in London in the early months of this year I undertook an experimental investigation of the disease by culture and animal inoculation. The results were of a negative kind, with the exception of the case of one rabbit that was inoculated with the citrated blood of a man suffering from typical glandular fever.

Disease of Rabbits following Inoculation of Human Blood.

This rabbit (CL 320) developed a condition characterised by fever, leucopenia, and anæmia. Fever, between 105° and 106° F., and anæmia with signs of ill-health and wasting, began between the eleventh and twelfth days after inoculation, and lasted until the twenty-second. Thereafter the rabbit became well again and appeared to make a complete recovery. By means of the citrated blood of this rabbit, taken

on the sixteenth day at the height of the fever, this condition was readily transmissible to other rabbits, and has been carried through eight passages, including in all 21 animals that have contracted the disease.

Apart from the first two passages, which showed some unusual features, the course, symptoms, and post-mortem appearances of this disease have been remarkably constant,

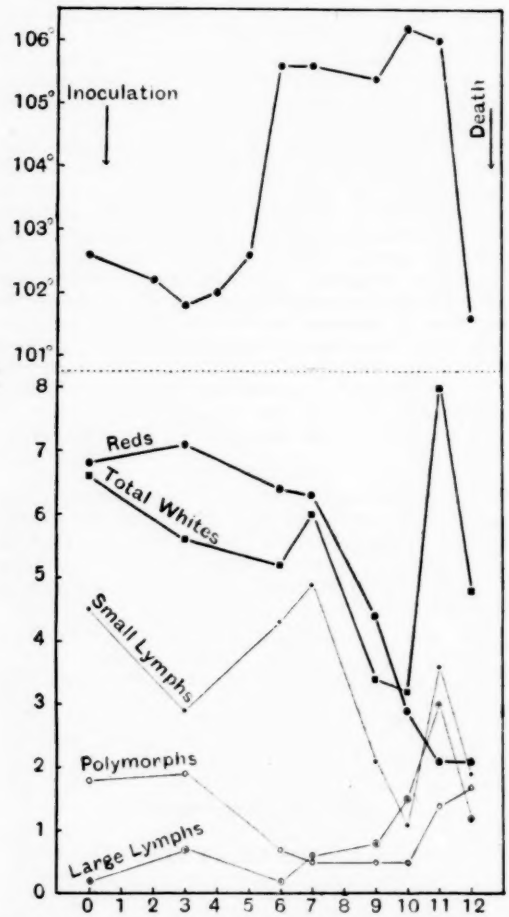

Chart of temperature and blood picture. The ordinates refer to days after inoculation, the abscisse to total number of cells per c.mm. in millions for red cells and thousands for whites. Large lymphs include monocytes. The upper half gives the temperature in degrees Fahrenheit with the thermometer 6·5 cm. in the rectum.

and are of the following nature: There is, first, an incubation period during which the rabbit seems well, and the temperature remains at its normal level, which may vary in individual cases from about 101°–103° F. During this period the erythrocyte count normally shows a slight increase, while the leucocytes remain fairly steady in both absolute and relative numbers. There follows an abrupt rise of temperature, which in one or two days reaches 105–106·5° F., where it remains some three to six days. During this febrile period the animal swiftly deteriorates, and it becomes thin, weak, apathetic, and short of breath, and looks extremely ill. The red cells fall rapidly to between two and three millions, and there is a leucopenia with an absolute increase of monocytes and, sometimes, of large lymphocytes. The terminal period is ushered in by a rapid fall of temperature to a normal or subnormal level, and the animal dies between the tenth and twelfth days after inoculation. A terminal leucocytosis has once or twice accompanied this period, but leucopenia is the rule.

The most constant features in the symptomatology are the incubation period, the rapid rise and rapid fall of temperature, and the rapid fall of the erythrocyte count. The white cells do not show such constant variations, and for the diagnosis of the experimental disease it has been found that a combined red cell and temperature chart is sufficient. An illustrative chart of temperature and blood picture is given on this page; the actual figures of the blood counts in the table. This chart and table refer to rabbit CL 348 of the fifth passage. The animal was inoculated on July 5th with 7 c.cm. of infected blood by the intravenous route. It presented typical symptoms, and died during the night of July 17th and 18th. At the post-mortem there was the typical enlargement of spleen and liver with focal necrosis, but the glands were not enlarged.

Table of Counts made on Blood taken from Ear-vein of Rabbit CL 348.

Date in July, 1930.	Erythrocytes.	Leucocytes.	Polymorphonuclears.	Eosinophils.	Basophils.	Small lymphocytes.	Large lymphocytes.	Monocytes.
	Per c.mm.		Per cent.					
5th ..	6,787,000	6600	25·5	0	2·5	68·5	1·5	1·0
8th ..	7,100,000	5600	29·5	0	4·0	52·5	6·0	8·0
11th ..	6,450,000	5200	12·5	0	2·0	82·5	1·0	3·0
12th ..	6,325,000	6000	7·0	0	1·5	81·5	2·0	8·5
14th ..	4,375,000	3400	12·5	1·5	1·5	61·5	2·0	23·0
15th ..	2,937,000	3200	14·0	0	1·5	35·5	1·5	46·0
16th ..	2,112,000	8000	14·5	0	3·5	44·5	1·0	36·0
17th ..	2,152,000	4800	31·0	0	5·0	39·5	2·5	22·0

POST-MORTEM FINDINGS.

Post mortem in this disease one finds considerable wasting, and there is little fat in the subcutaneous tissues or mesentery. The *peritoneum* contains no excess of fluid and is normal. The *spleen* is greatly enlarged—a typical one measured 7·5 × 1·9 × 1 cm., and weighed 6·6 g. The colour is a deep reddish-purple, the texture fairly firm. The organ is studded with large numbers of white nodules from pin-head size up to 0·4 cm. diameter. These are rather harder than the pulp, and when a piece of spleen is ground in the mortar the resulting paste is granular, like cod's roe, on account of them. The *liver* is usually enlarged and a pale brown in colour, with well-marked lobular pattern. It is studded throughout with yellowish-white flecks and nodules of irregular shape and size, from pin-head up to 0·4 cm. diameter. The *stomach* is normal, but the rest of the gut varies in appearance. It is sometimes normal, and sometimes shows signs of enteritis. In this connexion it must be noted that an epidemic of diarrhœa was present among the normal stock rabbits throughout this investigation. The other abdominal organs are normal, with the exception of the testicles in male animals, which are frequently very small and may measure only 2·6 × 0·6 × 0·7 cm. The *tongue*, *larynx*, *trachea*, *pleuræ*, and *pericardium* are normal. The *lungs* are frequently very pale, collapsed, and œdematous, oozing froth and blood-stained fluid from the cut surface on pressure. Once only were nodules found in them similar to those in the spleen and liver. The *heart* is normal. The *brain* is normal. The *marrow* of the femur is deep red and very soft and friable, and can only be peeled out from the cracked bone with difficulty. The *lymphatic glands* are in most

cases enlarged throughout the body, and sometimes show injection. Glands from the groin have measured 0·8×0·4×0·3 cm., as against the normal for this site of 0·5×0·2×0·1 cm. Of the post-mortem findings the enlargement and nodular condition of the liver and spleen is invariable. The glandular enlargement is less so. The other features are variable.

A detailed investigation of the history of the organs has yet to be completed, and the findings will be reported later. From what histology has been done it appears that the nodules in the spleen are massive focal necroses of the pulp, around which there is little reaction. The lymphoid tissue is little affected, and the organ contains much blood and appears to be stuffed with red cells. In the liver there are also foci of necrosis, and there is more or less proliferation of the reticulo-endothelial cells around the portal spaces, which are infiltrated with lymphocytes. The condition of the enlarged glands is interesting for its resemblance to that of human glands from cases of glandular fever—namely, that there is a proliferation of the reticulum cells and the cells of the lymph sinuses. This is not as marked as in the human glands, and the more acute nature of the disease in rabbits may account for this. In some of the glands there are foci of necrosis surrounded by a zone of proliferated reticulum cells.

Attempts to cultivate an organism from the blood and organs of these rabbits have failed. On six occasions blood used for passage with a positive result has been cultured by a variety of aerobic methods, and on five of these it was sterile. On the sixth was obtained a Gram-positive spore-bearing bacillus with a spreading, dry, arborescent habit of growth on agar—an obvious air contaminant. Organs from 11 cases have been cultured by aerobic methods, and in the majority of cases have been sterile. Where organisms have been grown they have either been of an intestinal type, presumably agonal invaders, or else obvious air contaminations. No one type of organism has been constantly present. Further attempts to grow the infective agent will be described later.

Nature of the Disease.

The question arises whether this condition (which for convenience and without any pre-judgment of its true nature will be spoken of as experimental glandular fever) is identical with the human disease or whether it is a natural disease of rabbits that was aroused by the inoculation of human blood. Two conditions have been described which resemble it more or less closely: (1) Infection with the *Bacterium monocytogenes* of E. G. D. Murray, R. A. Webb, and M. B. R. Swann[1]; and (2) the natural disease of hares described by K. Aoki, S. Kondo, and J. Tazawa,[2] which is due to a filtrable virus and which is infective for man, rabbits, guinea-pigs, and mice.

1. The presence of a monocytosis, focal necroses in the liver and spleen, and enlargement of the lymph glands are common to intravenous injection with *B. monocytogenes* and with experimental glandular fever blood, but here the resemblance ends. In *B. monocytogenes* infection there is a leucocytosis, the serous cavities almost always contain a large amount of exudate, and the subcutaneous tissues are often œdematous. On the other hand, leucopenia is the rule in experimental glandular fever, and exudates in the serous cavities and œdema of the subcutaneous tissues have never been seen. Moreover, in the fairly extensive series of cultures made from infective blood and from the organs post mortem the *B. monocytogenes* has never appeared. It may be taken as improbable that there is any relationship between the two diseases.

2. The disease described by Aoki, Kondo, and Tazawa causes in man a fever of short duration, followed by painful swelling of the lymph glands. In rabbits it produces a high fever which is rapidly fatal, and there are sometimes, but not regularly, enlargement of the spleen and liver, with the presence of submiliary nodules, and swelling of the lymph glands. Nodules were most common, however, in the peritoneum, and were often so numerous as to cause a matting together of the abdominal organs. In experimental glandular fever no case has been seen with nodules in the peritoneum, while they have been constantly present in the liver and spleen. Aoki, Kondo and Tazawa were able to cause their disease not only with infective blood but also with suspensions of organs, but attempts to do so with experimental glandular fever have so far failed. Spleen has been tried four times, liver twice, and brain once. Aoki, Kondo, and Tazawa do not record the blood picture in their cases nor the histology—at any rate in their German papers. In the absence of these it is difficult to assess the relationship of their disease to experimental glandular fever, but if the two conditions are related they do not seem to be identical.

[1] Jour. Path. and Bact., 1926, xxix., 407.
[2] Centr. bl. f. Bakt., 1928, cv., 252.

There remains the possibility that experimental glandular fever is a natural disease of the rabbit, hitherto undescribed, that was aroused by the intravenous inoculation of human blood. To test this possibility four normal rabbits were inoculated with four normal human bloods. None of these rabbits showed any sign of disease. One, however, died seven days after inoculation from hæmopericardium following cardiac puncture. Of four further normals inoculated with the bloods of the previous rabbits one died, after two days, of enteritis, and there were no signs of experimental glandular fever; another died after three days in similar fashion; the third died after 19 days, also of enteritis, having shown no signs of experimental glandular fever during life or post mortem. The fourth animal remains alive and has been normal throughout. These three unsatisfactory deaths make it imperative that further controls should be done.

It is obviously impossible at present to conclude that the experimental and the human disease are the same. That experimental glandular fever followed the inoculation of the blood of a human case; that it is a disease characterised by fever and by swelling of the lymph glands; that it causes a profound disturbance of the blood picture; and that the histology of the enlarged glands shows features resembling human glands from glandular fever suggest the identity of the two diseases. On the other hand, it must be recognised that experimental glandular fever has been obtained from the blood of only one human case. The bloods of four other cases have been tried without success. Of these cases, however, three were possibly non-infective, since they had been ill some time and were afebrile when the blood was taken. The remaining case was early and febrile. The rabbit that received the blood (CL 321) showed a short period of low fever between 104° and 105° F. for seven days, and aborted on the third day of fever. Coincident with the febrile period there was a slight fall in red and white cells, but the picture was insufficient to suggest at the time an attempt at passage with the blood, and the opportunity was unfortunately missed. The temperature chart and blood picture are now seen to be suggestive of experimental glandular fever.

In order to settle the question of the identity of the human and experimental diseases, blood from further acute cases in the febrile stage is wanted and will be examined when it is available. This investigation and others on the nature of the infective agent, on its viability, cultivation, and filtrability, and on the histological features of the disease will be reported in subsequent papers.

Summary.

1. Inoculation of the blood from a human case of glandular fever into a rabbit was followed by a disease which is transmissible to other rabbits by the

citrated blood. 2. This disease is characterised by fever, anæmia, leucopenia, and monocytosis, enlargement of the lymph glands, spleen, and liver, and the production of focal necroses in them. 3. The relationship of this disease to human glandular fever is discussed. 4. The name "experimental glandular fever" is suggested for the disease in rabbits.

My thanks are due to Dr. S. P. Bedson for his advice throughout this investigation, and to my clinical colleagues for access to their cases.

CLINICAL AND LABORATORY NOTES

AN APPARATUS DESIGNED TO DIMINISH THE INCIDENCE OF POST-OPERATIVE THROMBOSIS.

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In The Lancet of July 12th appears a short article by Dr. C. A. J. Quant (Holland) entitled the Prevention of Thrombosis. Dr. Quant lays stress upon the "slowing of the blood stream as one of the most important of the possible causes of coagulation," and also indicates that the lower abdomen (especially the left side) is probably the usual site of the thrombosis. In recent years Waltman Waters, of the Mayo Clinic, has written on the subject of fatal pulmonary embolism, and in *Surgery, Gynecology, and Obstetrics*, January, 1930, will be found a modern summary of the methods of reducing its incidence. Dr. Waters states that at the Mayo Clinic the average incidence of fatal post-operative embolism from 1917 to 1927 was 0·34 per cent. The result of "the use of a regimen directed towards increasing the rate of metabolism, of blood pressure, and of blood flow in 4500 major surgical procedures of comparable type (to those of 1917 to 1927) during the last 4½ years has been followed by an incidence of fatal pulmonary embolism in less than 0·09 per cent. of cases." This is indeed a wonderful record and it is of interest to recall the means adopted.

Eliminating the bad risks which, of course, can be and will be guarded against, the method in use at the Mayo Clinic appears to be: 1. The decrease of metabolism and of blood pressure and the slowing of the circulation are combated by giving tablets of desiccated thyroid gland grs. 2 three times a day. 2. Patients are urged to move in bed, flex arms and legs, and especially to turn themselves from side to side (Wilson-Pool).

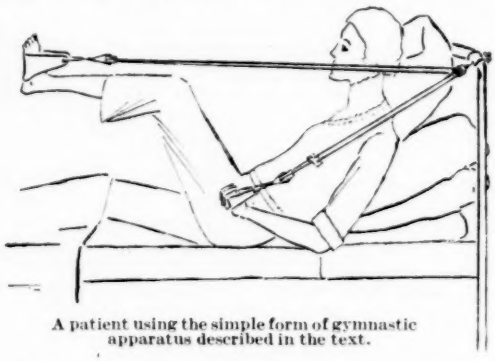
In a discussion following the presentation of Waters's paper Dr. Miller, of Chicago, stressed certain additional points: (1) careful pre-operative study, especially in old people, and the administration of digitalis as a cardiac stimulant; (2) careful operative technique; (3) particular attention to the fluid intake; (4) avoidance of tight bandages, especially near the chest; (5) systematic exercises, and especially daily elevation of the foot of the bed.

Dr. David, of Chicago, commented on the apparent increase in the frequency of the condition; in America it appears to vary from 1 to 3 in 1000 cases, and in Germany there has been an extraordinary increase during the last seven years. Has such an increase occurred in this country? It is very difficult to get any statistics from hospitals, because the cause of mortality is rarely given. My own impression is that there has certainly been an increase in private practice, probably entirely due to the "perfection" of modern nursing. I do not think the catastrophe ever occurred so frequently in hospital, where patients had to "fend for" themselves, and I do not think it is anything like so frequent now.

POST-OPERATIVE EXERCISE.

I have tried the thyroid treatment for the last two years, and regretfully say I have still had catastrophes. For many years I have advocated almost an "ambulatory" post-operative regimen—particularly in prostate cases—and I have been very pleased with it, both for the early closure of the wound and for freedom from thrombosis. One cannot, however, apply the "ambulatory" treatment to a gall-bladder or a stomach case, or after a big lower abdominal operation.

During the last 18 months I have been using in my private practice a very simple form of gymnastic



A patient using the simple form of gymnastic apparatus described in the text.

apparatus. There are three pulleys, one (double) at the head and one each (single) at foot and hand. The apparatus is fixed to the head rail of the bed, and is used first on one side and then on the other. A light cord is treaded through the pulleys as shown in the sketch, and there is a means of lengthening or shortening the length of the cord. The stirrup and handle are of soft, well-padded canvas. We use it for all abdominal operations, beginning as a rule on the fourth day. Some patients will try it earlier and others cannot and will not use it until later; some will not use it at all. At the beginning the patients can only exercise for about two minutes, but the time soon arrives when they are able to work the apparatus for five minutes at each side. In some cases they enjoy the exercise very much indeed, and will ask for it and work it for longer periods. The idea underlying the exercises is to prevent stagnation of blood, especially in the pelvis and lower abdomen. By pushing with the hand the leg is pulled well up to the abdomen and at the same time very good exercise is given to the arm. In practice it is found that the patient is best in the position shown in the sketch, and under these conditions there appears to be little if any painful drag on the abdominal wound. We find people who have assiduously carried out these daily "jerks" are not only happier for it whilst in bed but that when the time arrives to get up they are much more able to move about.

The apparatus is designed to "force" a patient into systematic activity at an early stage in recovery. It is to simulate the enforced movements which must be made in a hospital—to negative, if you will, the bodily comfort so ably dispensed in modern nursing. Done under the guise of "physical jerks" the exercises offer a very considerable temptation to most of our patients, and particularly to that class who need it most. The apparatus is made for me by Chas. F. Thackray, of Park-street, Leeds.

PURPURA SIMULATING THE ACUTE ABDOMEN.

By Ian Fraser, M.B., M.Ch. Belf., F.R.C.S. Eng. and Irel.,

Assistant Surgeon, Belfast Hospital for Sick Children.

Purpura has always been recognised as a disease by which a reputation could be made or marred. The text-books stress the point, and probably every surgeon who has opened many children's abdomens has at some time fallen into the trap. For two cases of purpura to occur within a week or so of each other in the same hospital, and for both to be operated upon, is, I think, sufficiently interesting (or distressing) to merit publication.

Case 1, a small boy, between 8 and 9 years old, was brought to hospital with a 12-hour history of abdominal colicky pain, intermittent in character, with the passage of blood. No tumour was palpable by abdominal examination. He had vomited several times, his pulse had mounted, and his temperature was subnormal. By artificial light his body appeared, without intimate inspection, to be normal. On rectal examination the finger was found to be covered with blood; considering his age, the history, the temperature, the presence of vomiting, and the rectal findings—notwithstanding the absence of the sausage tumour and the *signe de Dance*—a diagnosis of intussusception was made with confidence. Mr. H. P. Hall operated; free fluid was found in the peritoneal cavity, and the gut wall and mesentery were studded with petechial hæmorrhages and ecchymosed patches. The appendix was removed and the wound closed in layers without drainage. The child made an uneventful recovery and convalescence. Careful examination later revealed many minute small hæmorrhagic points which had escaped notice with artificial light. These pin-point hæmorrhages were more marked during the convalescent period.

Case 2 was equally interesting, especially as it followed closely on the first case, which had made everyone on the alert for the possibility of purpura. The patient, a little girl of 12, was admitted in the late afternoon with a history of having been taken ill two and a half days previously with generalised abdominal pain, followed some hours later by vomiting; for the last 24 hours the pain had been in the right iliac fossa. On examination by artificial light her pulse-rate was 120, her temperature 97° F., her tongue was dry and coated, and her breath foul. The abdomen was tender all over, especially over the appendix, and definitely rigid over McBurney's point. The chest and heart were normal. A rectal examination revealed a tender mass in the cæcal region. She thought she felt more comfortable since the morning; this ease had come on fairly rapidly. The only item of interest was that she thought her left foot and right wrist had swollen the last day or two, but there was nothing gross to be seen in them. Her urine was normal.

The diagnosis of acute gangrenous appendicitis was made, and I was rather inclined to think that it had perforated, considering the facts that she had become very much easier, that the pulse-rate had risen and temperature fallen, and also that the tongue was very dry and furred. She had been ill two and a half days, and was now rigid.

A muscle-splitting gridiron incision was made in the right iliac fossa under chloroform and ether. A large quantity of non-purulent blood-stained fluid escaped. The last two feet of the ileum were brilliant scarlet in colour and showed numerous small black areas of hæmorrhage. The gut wall was markedly thickened with the blood contained in the tissues, a condition which, I suppose, explained the mass felt per rectum. The hæmorrhage stopped more or less abruptly at the ileocæcal valve, leaving the cæcum almost normal. The appendix—perfectly harmless and beyond reproach—was removed. It was normal in every respect except that it contained a rich supply of thread-worms. The rest of the ileum was mottled, the mottling gradually decreasing towards the jejunum. There were several enlarged mesenteric glands, some soft and others calcified. An examination of the abdominal viscera through this limited incision failed to reveal any further pathology. The abdomen was closed in layers, with a small wick drain to allow the blood-stained fluid to escape.

Recovery was complete and convalescence normal, except for the following incidents. For three or four days after the operation the motions were mixed with dark blood, and on the third day the urine was heavily tinged with blood. The post-anæsthetic vomit contained blood and the saline returned after operation was also tinged. On about the tenth day she had a severe attack of epistaxis, and about the same time a marked purpuric rash appeared, involving both feet and the outer sides of the ankles. This was so severe that the feet were almost blue. There was also considerable swelling of the ankles.

A blood examination made after the operation was as follows: Blood film—marked preponderance of mononuclear cells. Differential count: mononuclears 35 per cent.; large lymphocytes, 22 per cent.; small lymphocytes, 8 per cent.; polymorphonuclear leucocytes, 35 per cent. Coagulation time, five minutes. Blood-platelets, 114,000 per c.mm. Red blood cells, 5,500,000. White blood cells, 16,500.

These two cases are of interest, in that the internal manifestations were well marked while outward signs were absent or slight. That two such cases should occur within such a short time is worthy of note, and that both should be operated upon merely lends support to the fact that purpura can simulate the acute abdomen very closely. In the two examples quoted it will be seen that the main external diagnostic signs of purpura were well marked after the operation, although almost absent before.

Although both children were operated upon at a time when they certainly had a tendency to bleed, there were no troubles of any sort with wound-oozing or hæmatoma formation. Both wounds healed well; the second showed a slight keloid formation.

TRIKETOHYDRINDENEHYDRATE

AS A REAGENT FOR ALBUMIN, PEPTONE, AND AMINO-ACIDS.

By Hermann Gardner, D.Sc.,

Head Dispenser, Queen Mary's Hospital, Stratford.

During an investigation involving the application of tests for proteins and amino-acids, I used a reagent discovered by Ruhemann and advocated in text-books,[1] which has found some usage in clinical laboratories—namely, triketohydrindenehydrate, or ninhydrin. It was noticed that, whilst ninhydrin gave positive indications, no confirmation could be obtained with Millon's reagent or by the biuret or xanthoproteic reactions, nor could amino-acids be isolated by acidulation and esterification in the usual manner. Baumann and Schotten's reaction also failed to reveal the presence of amines. This apparently paradoxical behaviour seemed only to be explicable on the assumption that the ninhydrin reaction was produceable by other than the products of hydrolysis of proteins.

A series of experiments was conducted with dilute ammonium salts in feebly alkaline solution (0·2 to 0·4 per cent. NH_4NO_3 or $(NH_4)_2SO_4$ and 0·04 to 0·1 per cent. $NaHCO_3$). Attention was arrested by the colour reaction these solutions afforded with ninhydrin, mostly a purplish red, which gave the distinctive blue on the cautious addition of very dilute hydrochloric acid. Reference to the published monographs of Harding and Warneford,[2] and of Harding

and MacLean,[3] confirmed the observation to a certain extent—namely, that "all ammonium salts *under the right conditions* are capable of giving the ninhydrin reaction. These conditions *appear* to be a faint alkalinity of the solution." (The italics are mine.)

Actually, alkalinity tends to produce a magenta or purplish red coloration rather than the typical blue, which only appears, as stated, on nearly neutralising the solution. Free ammonia in some amount appears to interfere with the reaction. It seems as if the colorations noted result from ammonium hydroxide in too great amount (although actually but small in proportion) masking the true (or blue) colour resulting from the interaction of NH_3 ions and the reagent. That the interaction is due to ammonia in the ionised state is indicated by the fact that an ammonium salt in very dilute solution will not react with ninhydrin even on boiling, but if a trace of sodium carbonate be added, the blue colour is produced on the addition of the reagent.

An ammonium salt in solution in the presence of alkali, in however small a quantity, indubitably undergoes partial—if but minute—decomposition, and the extreme dilution of itself tends towards ionisation.

If the hypothesis advanced is correct, obviously the presence of ammonia (NH_3) itself in minute amount in an aqueous medium should yield the distinctive reaction. Numerous solutions were prepared and tested, commencing with 0·5 c.cm. of ammonia solution (sp. grav. 0·888 at 15° C.) in 500 c.cm. of ammonia-free distilled water. This gave a claret-red solution on boiling with 1·0 per cent. ninhydrin, the fine blue colour associated with the test developing on the careful addition of N/100 hydrochloric acid. That the coloration was not due to ammonium chloride per se was subsequently proved.

Ultimately it was found that a dilution of 0·15 to 0·2 c.cm. of ammonia solution (sp. gr. 0·888) in 500 c.cm. reacted perfectly to the test—namely, 3 c.cm. of this dilution mixed with 1 c.cm. of 1 per cent. ninhydrin solution, boiled for two minutes, diluted with an equal quantity of distilled water and observed in a white glass tube of 8 mm. diameter by transmitted light, or against a white tile, exhibits the characteristic ninhydrin blue coloration. That is to say, water containing 0·00865 per cent. NH_3, or in 1 c.cm. 0·77 mg. NH_3 nitrogen, responds to the reaction.

SUMMARY.

Triketohydrindenehydrate is not a reliable reagent for the products of hydrolysis of protein generally. The colour reaction is almost certainly due to the presence of traces of free ammonia, or of NH_3 ions, and is masked by ammonium hydroxide (NH_4OH) or by alkali in excess.

Traces of alkali merely promote the reaction through causing the liberation of NH_3 ions from an ammonium salt. No doubt such ions appear amongst the hydrolysis products of protein in the presence of water, hence the reaction.

Ninhydrin, unlike Nessler's solution, is unaffected by ammonium salts in solution.

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2. Harding, V. J., and Warneford, F. H. S.: Jour. Biol. Chem., 1916, xxv., 317.
3. Harding, V. J., and Maclean, M.: Ibid., p. 339.

REVIEWS AND NOTICES OF BOOKS

A Text-Book of Hygiene.

By J. R. CURRIE, M.D. Glasg., D.P.H., M.R.C.P. Edin., Professor of Public Health in the University of Glasgow. Edinburgh: E. and S. Livingstone. 1930. Pp. 844. 27*s*.

A Synopsis of Hygiene.

Third edition. By W. WILSON JAMESON, M.D., M.R.C.P., D.P.H., Barrister-at-Law, Professor of Public Health, London University; and G. S. PARKINSON, D.S.O., M.R.C.S., L.R.C.P., D.P.H., Assistant Director of Public Health Division, London School of Hygiene and Tropical Medicine. London: J. and A. Churchill. 1930. Pp. 541. 18*s*.

Prof. Currie's new text-book is intended for medical students engaged in studying hygiene, but is also meant to be of service to candidates for the diploma in public health. In the range of subjects dealt with it should more than satisfy the present requirements of any examining body for a medical qualification, and will go a long way towards meeting the more detailed wants of the post-graduate student. The sections on air and ventilation, warming and lighting, soil, water-supply, refuse, and sewage disposal are well written and free from many of the obsolete notions which too often make their appearance even in first editions. The question of river pollution is well reviewed and the events which have led up to the present unsatisfactory position are briefly summarised. The public health law (both English and Scottish) is described fully in each section, an arrangement which is convenient for the student. A short summary of the Local Government Acts of 1929 for both countries is also included. The chapter on epidemiology is comprehensive, noting the main theories of the epidemic which have been put forward since the time of Hippocrates, and including a reference to the modern experimental work of Topley and Greenwood.

There are certain omissions and defects which deserve comment. No reference is made either to the dangers of polluted swimming baths or to the practice of continuous filtration which has now been so widely adopted in public bathing installations. The sections dealing with maternity and child welfare and school hygiene are disappointing. Amongst the subjects requiring more detailed consideration are nursery schools, the duties of health visitors, and the provision for physical and mental defect in school-children. Except for a passing note the important subject of mental hygiene is ignored. A bibliography might have been useful, especially since some dogmatic statements made are not in accordance with accepted teaching. The standard of allowable respiratory impurity set out differs from that of de Chaumont, and a rather sweeping assumption concerning the capacity of crevices and chinks as air inlets is put forward. No authority is quoted for the estimate of 3 per cent. as the incidence of chronic carriers of amœbic dysentery in the United Kingdom. Generally, as in most text-books of hygiene, even those purporting to be modern, there is too much bias on the environmental hygiene side compared with the manifold problems of individual hygiene which

to-day form so large a part of the work of a public health department.

In many other respects the book is well up to date, references to psittacosis, undulant fever, post-vaccinal encephalitis, the serum treatment of anterior poliomyelitis and measles are included. The subject of statistics is adequately dealt with, and the review of statistical methods should be sufficient for candidates for degrees or diplomas in public health.

The new edition of the popular synopsis of hygiene, in the preparation of which Lieut.-Colonel Parkinson takes the place of Mr. F. W. Marchant as Prof. Jameson's collaborator, includes reference to the more outstanding changes in public health administration which have taken place since the appearance of the second edition. Of these, the most important and far-reaching is, of course, the Local Government Act, the main provisions of which are briefly set out. The recommendations of the Ministry of Health Committee on Vaccination and the provisions of the Vaccination Order, 1929, are also noted and the instructions to vaccinators contained in the first schedule of the Order are given in detail. The provisions of the Food and Drugs (Adulteration) Act, 1928, are well summarised. The whole work bears evidence of being thoroughly revised and brought up to date. The authors do not claim that the book is anything but a synopsis, but the reader will find that it is also a very useful index to modern public health literature. The section on vitamins is an admirable résumé of the present position. The chapter dealing with vital statistics has been rewritten and is one of the best in the book.

Treatment of Children's Disease.

By Prof. F. LUST (Karlsruhe). Translation of Sixth edition with additions by SANDOR A. LEVINSOHN, M.D. (Paterson, N.J.). London: J. B. Lippincott Company. 1930. Pp. 513. 30*s*.

ALTHOUGH text-books of pædiatrics are numerous, surprisingly few are devoted exclusively to treatment. Prof. Lust's work has proved its popularity on the Continent. This volume is something more than a translation of the sixth (German) edition, since it has been supplemented by additions made by the author, representing the advances of the last three years, and also by the translator, introducing modifications in accordance with current American practice. The first half of the book deals with individual diseases, a short diagnostic summary being followed by an account of the management and treatment of each disorder. The second part, arranged in alphabetical order, is devoted to drugs and formulæ, including preparations used in infant feeding. Close printing and a condensed style have made the volume more comprehensive than its size suggests, and it should be of considerable service to practitioners.

Diagnosis and Treatment of Heart Disease.

Practical Points for Students and Practitioners. Sixth edition. By E. M. BROCKBANK, M.D. Vict., F.R.C.P., Hon. Consulting Physician, Royal Infirmary, Manchester. London: H. K. Lewis and Co., Ltd. 1930. Pp. 240. 7*s*. 6*d*.

THIS little book is full of useful information. In addition to the usual subject matter found in volumes on heart disease, many practical points of real clinical importance are included. For example, in discussing the cardiac impulse and the apex-beat the author says, "remember the extension outwards of the impulse of a nervous rapid normal heart." He advises that three blood-pressure readings should be taken on every patient, since the first inflation of the armlet is liable to induce some spasm in the artery, especially in apprehensive subjects with quick pulses, leading to too high a reading; many other examples of a similar kind could be given. On the vexed question of the significance of the systolic murmur Dr. Brockbank would have us believe that whenever this is found to be present it is evidence of mitral regurgitation due either to disease of the valves or dilatation of the valve ring; in this his teaching differs from that now widely accepted, that a murmur which is found alike in health and disease cannot have the same significance in every case. The chapter on the heart in school-children is a valuable one; it is good to see stated a fact which is so seldom realised—that the impulse of the contraction of the left ventricle in children below puberty can be outside the nipple line. Equally useful is the chapter on examination for life insurance; the advice to listen to a doubtful heart with the patient lying down as well as standing could usefully be followed in all examinations of the heart. The main criticism to be levelled against this book is that insufficient space is given to important recent developments in diagnosis and treatment of cardiac disease. For example, coronary thrombosis is not given the notice it deserves, and only a scanty paragraph is devoted to the use of the X rays in diagnosis. Dr. Brockbank has, however, offered innumerable practical hints of great value.

Medical Science for All: Man v. Microbes.

By NICHOLAS KOPELOFF. New York: Knopf. 1930. Pp. 319. With 130 figures. 21*s*.

THIS attempt to popularise microbiology is not a great success. It has the worst fault of popular scientific exposition in being ecstatic and exaggerated. The title itself is misleading, for man actually gains much more by the kindly offices of some microbes than he loses by the attacks of others. The first sentence of the preface—"a man is only what his microbes make him"—is nonsense. The book is, moreover, unsound in detail. "Galloping consumption" (p. 105) is not general miliary tuberculosis; oysters (p. 121) do not "float" in sewage when being fattened; de Morgan (p. 197) did not initiate the rhyme about "great fleas have lesser fleas" which dates back at least as far as Jonathan Swift; the precise statements on p. 202 of the minimal fatal doses of toxins for man have no justification; and on p. 176 there is a complete muddle about *Leptospira icterohæmorrhagiæ* and the state of knowledge of the causation of yellow fever at the time of Noguchi's death. In short, the layman who wants to know something about bacteriology will find sounder information at less cost in the Home University Library.

Études sur les maladies familiales nerveuses et dystrophiques.

By O. CROUZON, Physician to the Salpêtrière. Paris: Masson et Cie. 1930. Pp. 385. Fr.55.

COLLECTED into a convenient volume the reader will find a valuable series of papers written during a period of years by Dr. O. Crouzon, all of which bear on questions of familial, in distinction to hereditary, nervous and dystrophic disease. They range widely over the whole field and include both the banalities and the rarities. The intrinsic value of some is considerable; for example, the articles dealing with cleidocranial dysostosis and craniofacial dysostosis

are highly informative, as well as being excellently illustrated, and the same may be said of those devoted to familial ocular affections. Here the neurologist will discover unfamiliar facts of much interest. Similar minute and clear description characterises other chapters concerned with cerebellar atrophies, lenticular degeneration, Friedreich's disease, and myoclonus epilepsy. When, however, the reader seeks instruction beyond the plane of clinical medicine he early becomes conscious of our limitation of knowledge. Dr. Crouzon has endeavoured to work out the application of Mendelian principles to familial disease, collecting from personal observation and the literature the records of numerous families in which disease has appeared on a larger or smaller scale; and in most instances he is compelled to state that the paucity of data prevents definite conclusions from being drawn. He considers, none the less, that in Huntington's chorea, cerebellar heredoataxia, and hypertrophic neuritis Mendelian proportions are observed, and he asserts that they are likely to be found present also in Thomsen's disease, Friedreich's disease, familial tremor, retinitis pigmentosa, familial nystagmus, and periodic family paralysis.

Annals of Roentgenology: The Neck.

Vol. IX. By PERCY D. HAY, Jnr., M.D. New York: Paul B. Hoeber. 1930. Pp. 104. $8.

IT is usual in radiological studies to take an organ or a system and work out the radiology applicable to it. Dr. Hay's method of taking an anatomical region, comprising parts of many systems, is unusual if not unique. It certainly has advantages. The author has worked in a department that serves Dr. Chevalier Jackson's bronchoscopic clinic. This service calls for the utmost detail in the radiological examination of the neck, lest some unsuspected foreign body or pathological lesion should be present, and the number and variety of conditions met with are astonishing. Dr. Henry K. Pancoast, in an introduction, points out that the perusal of Dr. Hay's manuscript brought home to him and his fellow workers the importance of a careful study of the neck of every child submitted to examination for suspected enlargement of the thymus gland—a condition which would appear to be much more common in North America than in this country. The author devotes a special section to the examination of the neck in suspected thymus cases, since high respiration disturbance may be due to non-opaque foreign bodies in the trachea, diphtheria, intratracheal or intra-œsophageal abscess, which must all be excluded before the thymus is incriminated.

The atlas is based on a detailed study of 203 cases, 128 of which were pathological, the remainder being normal children and adults. Fourteen different pathological conditions were met with in the series and these are fully described. The radiography of infants is always difficult and, since dyspnœa is present in so many of the conditions illustrated, to obtain any radiographic result at all is a feat of management and skill. When we think of the difficulties that must have been encountered Dr. Hay deserves praise for his achievement in collecting such a representative series; the radiograms illustrating the various lesions in adults, particularly the stenotic conditions, are exceedingly good.

Although this volume is smaller in scope than its companions it is worthy in every way to take its place in this excellent series of monographic atlases.

INTERNATIONAL CONGRESS OF PÆDIATRICS.

STOCKHOLM, AUGUST 18TH–21ST.

(FROM OUR OWN CORRESPONDENT.)

SOME 600 specialists, representative of countries from America to Japan, attended this Congress, the proceedings of which are to be fully reported in a special volume of the *Acta (Scandinavica) Pædiatrica*, which will contain abstracts in English, French, and German. The organisation of the Congress was admirable, and its success was principally due to the industry and courtesy of the Swedish National Committee, whose president was Dr. I. Jundell, and secretary Dr. Nils Malmberg.

Biological Effects of Irradiation.

It may perhaps surprise English practitioners, who regard rickets as no longer a common disease, that over a third of the time of the Congress was devoted to a discussion on the biological effect of direct and indirect ultra-violet irradiation, with particular regard to rickets. Alfred F. Hess (New York) opened with a paper on the indication for these therapeutic radiations, emphasising their importance in rickets, tetany, and osteomalacia. They were of possible value in dental caries, but in other conditions—for example, coryza and respiratory affections—he held them of no avail and possibly harmful. He drew attention to the importance of using an accurately standardised preparation of ergosterol, especially in experimental work upon the subject. In the discussion which followed the methods of standardisation were criticised on the ground that rickets in rats could not be compared closely with rickets in man. It was suggested that the use of a radiation, screened to give a short band of the spectrum, would produce a purer brand of ergosterol. Faber and Bloch (Copenhagen) emphasised the distinction between hypocalcæmic rickets, associated with tetany and osteoporosis, and hypophosphatæmic rickets with marked bony overgrowth and deformity. H. J. Gerstenberger (Cleveland) considered that the high-phosphorus low-calcium form of rickets was becoming commoner owing to insufficient protection.

The Thymo-lymphatic System.

The general facts concerning the metabolism of calcium and phosphorus and their clinical significance were, apart from rickets, touched on rather lightly in the second session on the thymo-lymphatic system. The subject was opened by J. A. Hammar (Upsala), C. Cattaneo (Milan), E. Moro (Heidelberg), and G. Mouriquand (Lyon), who dealt chiefly with diagnosis. The existence of a clinical entity was agreed, but opinion varied whether the hyperplasia of the lymphatic system was a cause or an effect of some general metabolic factor, the balance being in favour of the latter view. It was also considered that *l'état lymphatique avec la mort subite* and the *diathèse exsudative* of Czerny, Paltauf, and others were but different grades of what in England is termed the exudative diathesis.

Psychopathology of Children.

The third subject of discussion was opened by R. D. Gillespie (London) and F. Hamburger (Graza) from different points of view. Prof. Hamburger made an effective plea that the pædiatrician should

not concern himself too exclusively with the child's body, for it was he who saw most of the psychopathic disorders at a stage when they were comparatively easy to deal with. He was in a position to observe their origins in early infancy, and to distinguish those that were inborn and those that were acquired as a result of early environment. He could mitigate or remove the handicaps encountered by the child when it was beginning to realise that the world contained other persons. Suggestion during the early years of life might determine the course that the child would eventually follow. Present-day physicians and students should attend to this aspect of their duty, although it was not associated with figures and percentages. Dr. Gillespie indicated the lines taken by psychogenic disorders in children, and the symptoms encountered. It was, he said, unwise to interpret the mind of a child in terms of the emotions of an adult, and he did not admit that infantile sexuality played the part in forming the mental make-up of a child sometimes ascribed to it. It was not impossible, he thought, to gain the partial confidence of a child in a clinic with others present; it was therefore desirable for students to attend such a clinic and see for themselves the types of symptoms that were amenable to treatment by the psychiatrist. In the psychopathies of childhood and adolescence the results obtained were equal to those of other branches of medical science. Benjamin (Munich) spoke of the importance of a consideration of the "stubborn phase" (*Trotzphase*) from two to four years of age; many of the neuroses in childhood had their roots, he claimed, in mismanagement at this period of a child's life.

Afternoon Discussions.

During the afternoons group discussions were held. At one of these Ernberg (Stockholm), Wallgren (Goteborg), Alfaro (Buenos Aires), and Johannsen (Goteborg), reported on their studies in *erythema nodosum*. Without exception they considered it to have a tuberculous origin in the majority of cases, the nodules being the manifestation of an anaphylactic reaction to a skin sensitisation. A source of infection could usually be demonstrated. Johannsen maintained that cases of unquestionable rheumatic ætiology were very rare in children, and that in these cases also it was an allergic reaction. Polyarthritic symptoms in association with erythema nodosum were not necessarily rheumatic; cases of acute polyarticular rheumatism with hot swollen joints, which were not pyogenic and did not react to salicylates, should be considered as allergic manifestations of tubercle.

L. G. Parsons (Birmingham) presented a study of the fat metabolism in cœliac disease, in which no evidence was obtained that the increased fæcal fat was due to increased excretion of blood fat. He considered the low fat curve to be the result of defective absorption from the intestine.

S. W. Davidson (Newcastle) described the radiological appearances of five cases of osteochondritis ischiopubica in children between five and eight years, and pointed out the clinical resemblances to early tuberculous hip-joint disease.

J. C. Spence (Newcastle) described 17 cases of nutritional xerophthalmia, and emphasised the significance of skin infections and epithelial cells in the urine as evidence of xerophthalmic diet deficiency. Spence's observations suggested also that the specific food factor involved was not the same as the growth factor or the anti-infective factor for general infections.

B C G VACCINE.

Several reports on the use of B C G vaccine were presented. W. H. Park (New York) said that if as a result of a long series of animal experiments a strain was cultured strictly according to the directions of Calmette there was no danger from increase of virulence. If the method did not provide effective prophylaxis in every case there was, he said, no doubt that a child vaccinated early and carefully protected from contact with tubercle for about two months gained a useful degree of protection against virulent infection in home surroundings. The appearance of a positive Mantoux test was, he thought, the best indication of developing immunity. Drucker (Copenhagen) reported the recovery of tubercle bacilli from the stomach in 100 per cent. of cases of Pirquet-positive children under one year of age. Among these was one child which had been vaccinated with B C G six months earlier, and from whom a bacillus identical with the Calmette-Guérin organism was recovered from the stomach washings.

INTERNATIONAL UNION AGAINST TUBERCULOSIS.

OSLO CONGRESS, AUGUST 13TH–15TH.

In the presence of the King and Queen of Norway, the seventh conference of the *Union Internationale contre la Tuberculose* opened at Oslo on August 13th with a service of music in which the orchestra played Greig's symphonic poem "Spring." Speeches by Prof. Th. Frölich (Oslo), president of the organising committee, and Prof. Léon Bernard (Paris), secretary-general, terminated the formal proceedings.

Preventive Vaccination.

A discussion on preventive vaccination against tuberculosis by means of the Calmette-Guérin bacillus was opened by Prof. A. Calmette (Paris) himself. Immunity against tuberculosis was, he said, determined solely by the presence in the body of living tubercle bacilli. B C G was a living strain of fixed characteristics hereditarily attenuated after more than 230 subcultures on a glycerinated ox-bile medium. It was entirely free from pathogenic characteristics and the presence of bile rendered it more capable of absorption by the intestine of infants. Although when introduced into animals in massive doses it might give rise to tubercles, these underwent regressive changes and disappeared without leaving any trace. The organism, he believed, passed easily through the intestinal wall, and provided the animal was isolated for at least a month from contact with an infectious case an immunity was produced in cattle which lasted for about 18 months—i.e., so long as the bacilli remained in the lymphatic glands. Subjects already infected by virulent bacilli derived no benefit from the vaccine. Prof. Calmette denied that the B C G strain could ever become virulent in the way suggested by S. A. Petroff and others; he regarded such events as the result of accidental contamination. The method had been practised since 1924 in many countries of the world, and a fall in the tuberculosis mortality (and also in the general mortality) had been observed among vaccinated as compared with unvaccinated children. He claimed the method as suitable for universal application.

Qualified support was given by F. Neufeld (Berlin), while W. H. Park (New York) and Heynsieus van den Berg (Amsterdam), from a series of 365 children, recommended the method as free from danger. The

remainder of the ten official speakers had nothing but praise for the method, and advocated its more general acceptance. Some comment arose on the use of the general infantile mortality as a test of the efficacy of the vaccine; L. Bernard said it had been adopted to give greater accuracy, since it was impossible during life to diagnose tubercle with certitude among children. E. A. Watson (director of the Animals Diseases Research Institute, Ottawa) was the principal critic of the method; he had obtained, he said, 36 per cent. of mild tuberculous lesions by the injection of B C G, more or less severe in 2–7 per cent. A. Kirchner (Hamburg) supported Petroff's view. A. Fontes (Brazil) said he had observed no ill-results in a series of over 4000 cases. A. Greil (Innsbruck) condemned not only vaccination but the theoretical conception of immunity. No speaker touched on the recent catastrophe at Lübeck; as the causes of that unfortunate affair are still under consideration by the German health authorities all reference to it was excluded by common consent.

Thoracoplasty.

On the second day, P. Bull (Oslo) reviewed the work done in Norway upon thoracoplasty in the treatment of tuberculosis. He limited its use to chronic cases with unilateral disease in which an attempt to collapse the lung had been made without success. The operation, he said, should be undertaken only after a prolonged period of observation and if the other lung showed no signs. He preferred to perform the operation in two stages; there was no particular difference in results between local and general anæsthesia. Nearly half of the patients who could not be cured by other means were restored to full working capacity.

F. Sauerbruch (Berlin) spoke from an experience of 1200 cases with 40–50 per cent. of cures in strictly unilateral cases. He preferred to operate in one stage under local anæsthesia with ½ per cent. novocain. J. Gravesen (Vejlefjord) said 45 per cent. of over 200 cases had been able to return to work. His operation mortality was 7½ per cent.; he preferred general narcosis with morphine and ether, supplemented by suitable local anæsthetic. H. Morriston-Davies (Ruthin) believed that a large extent of rib resection was only desirable in old fibrous cases; in others it was unnecessary and harmful. After experience of both methods he had reverted without hesitation to the one-stage technique; he preferred a combination of light chloroform anæsthesia with 1 per cent. novocain. The general trend of other papers was favourable to the method and the discussion centred on points of technique. H. Vogel-Eysern (Davos) made a plea for greater application of functional tests for lung capacity before operation.

Teaching of Tuberculosis.

On the third day a discussion on the teaching of tuberculosis to medical students and practitioners was opened by W. His (Berlin), who based his remarks on replies to a questionaire sent out to many universities. While admitting that division into specialties contributed towards our knowledge of medicine, he had been impressed with the danger to science in general by undue specialisation. In no university in the world, however, was the teaching of tuberculosis entirely divorced from that of general clinical medicine. In most centres there were short courses, accompanied by visits to sanatoriums, where in some places students were guests for a fortnight or so. There was, he said, a dearth of post-graduate courses; some were given over a series of week-ends, so that neighbouring practitioners might attend. In Canada courses were provided by a prominent insurance company; some governments and national associations also granted travelling scholarships for this purpose.

Dr. W. B. Soper (New Haven) spoke of post-graduate teaching in America; in places where there was an enthusiast ready and able to give up his time and influence to teaching there existed a flourishing school of tuberculosis. In other places, he said, progress was less evident; a general stimulus was required. Dealing with undergraduate teaching Sir Robert Philip (Edinburgh) said it was not sufficient to train a student so that he was merely able to recognise the well-marked cases of the disease when it presented itself. Tuberculosis was a social malady of vast dimensions, and it was more important to impress the student with the way in which it entered intimately into the medical history of so many individuals. Pulmonary phthisis was not the only form which the disease took, and attention was too closely centred upon it. Undergraduates, he had found, welcomed the subject when it was put to them from a biological standpoint. E. Morelli (Rome) described the new Mussolini Institute for Tuberculosis and Respiratory Diseases which is being built in Rome as an international research centre with accommodation for over 1200 patients.

The conference closed with a meeting of the general assembly of the Union. Upon the proposal of C. Mainini (Buenos Aires) a commission was appointed, with representatives from various countries, to consider the standardisation of nomenclature in tuberculosis. N. Heitmann (Government inspector of tuberculosis in Norway) gave a sketch of the development of tuberculosis work in Norway since the passage of the Act of 1900 which enforced notification and a system of treatment, and the part played in providing sanatoriums by the Norwegian Women's Public Health League started in 1896. Although since that date the fall of mortality in the towns amounted to nearly 50 per cent., the general death-rate for all forms of tuberculosis in Norway remains higher than that in Britain.

After the conference visits were paid to outlying sanatoriums, including that of Hagevik, near Bergen, admirable alike in situation and internal equipment.

The eighth meeting of the Union will be in 1932 in Holland, under the presidency of Prof. W. Nolen (The Hague).

SEAMEN'S HOSPITAL SOCIETY.—During the past year 6425 in-patients and 26,069 out-patients were treated at the various hospitals of the Seamen's Hospital Society, nearly half of them at the Dreadnought Hospital at Greenwich, 1538 at the Hospital for Tropical Diseases in Endsleigh-gardens, and 295 at the Queen Alexandra Memorial Hospital at Marseilles. The income was £93,578 and the expenditure £95,497. A new out-patient department and a complete theatre unit are needed at the Dreadnought Hospital at a cost of £35,000, and extensions and alterations at the Endsleigh-street Hospital are estimated at £20,000.

BRITISH DENTAL HOSPITAL.—The annual report states that the work at the treatment centres and clinics of the British Dental Hospital increases steadily. Larger buildings, better adapted and equipped, X ray apparatus, and research workers are needed, but cannot be supplied out of the fees charged to the patients. The centres at Camden-road, Lewisham, Tooting, and Hammersmith provide skilled dental treatment to persons not entitled to benefit under the National Insurance Acts, and another important branch of the work is the provision of dental facilities, in association with a number of metropolitan borough councils, for expectant and nursing mothers and young children. Last year 5273 children from London County Council schools were treated at the Lewisham centre, an increase of 458.

THE LANCET.

LONDON: SATURDAY, SEPTEMBER 6, 1930.

THE PHYSIOLOGY AND PATHOLOGY OF DIABETES MELLITUS.

In the Oliver-Sharpey Lectures, of which the second is published in our columns this week, Prof. J. J. R. MACLEOD has reviewed some of the experimental work designed to solve new problems which have arisen as a result of the discovery of insulin. The work was done mostly on depancreatised dogs which, though kept alive and well for a period by means of insulin, were found to die, as a rule, some eight months after the operation, with severe jaundice and fatty degeneration of the liver. The stools of the dogs always contained undigested muscle-fibres and a great excess of fat. On the assumption that the fatal issue might be due to lack of the external secretion of pancreas, Prof. MACLEOD tried giving the animals 2 oz. of raw pancreas a day. With this routine he was able to keep two dogs alive for four years, and but for an unfortunate accident it is probable they would have lived much longer. He suggests that the ability of dogs to survive may be determined by the presence of nodules of pancreatic tissue in the submucous layers of the duodenum. This hypothesis may explain the clinical observation that some patients with carcinoma of the head of the pancreas suffer much less from fatty diarrhœa than others on similar diets. Among other interesting observations was that on the effect of pregnancy. Dr. R. D. LAWRENCE has reported a case [1] which suggests that the fœtus may supply the pregnant woman with insulin during the last weeks of intra-uterine life. In Prof. MACLEOD'S experiments, however, the course of the pregnancy was quite normal, and the insulin requirements did not vary with the approach of full term. This observation renders improbable the hypothesis of fœtal supply, and another explanation must be sought for the change in the insulin requirements which has occasionally been reported during human pregnancy.

The symptoms following the withdrawal of insulin were carefully watched on several occasions, and one point which has an important bearing on clinical practice was noted. The fat animals developed on the fourth or fifth day a severe ketosis associated with vomiting, and died unless insulin was given; the thin dogs suffered much less from ketosis. By analogy, the diabetic patient who is fat is probably in much greater danger than a thin one if the insulin is omitted, and also if the dose is not increased promptly whenever the insulin requirements are greatly raised from any cause. The conditions which regulate the secretion of insulin from the β cells of the islands of Langerhans are fully discussed by Prof. MACLEOD. It has now been proved that stimulation of the right vagus nerve causes a decrease in the blood-sugar. This decrease is probably due to the secretion of insulin, but since we have no means of estimating the amount of insulin present in the blood, the relation cannot be accepted as certain. It is likely that the vagus centre is stimulated as the direct result of the increase in the blood-sugar. Prof. MACLEOD has tested the effect of some of the preparations which have been used as substitutes for insulin. Three substances, synthalin, myrtillin, and bile-salts have been tried, since experimental evidence that they have some effect on the blood-sugar is not lacking. Prof. MACLEOD concludes that synthalin does lower the blood-sugar of normal and diabetic persons, but is of no value in the treatment of coma. He finds that it can replace some 10 to 20 units of insulin, but that in view of its liability to cause toxic symptoms it is of little value in therapeutics. Myrtillin and bile-salts were found to have very little action on the blood-sugar, and none in depancreatised dogs; there seems, therefore, to be little justification for recommending them in the treatment of patients, and still less for prescribing for diabetics substances which have no action on the blood-sugar in any circumstances.

The study of Prof. MACLEOD'S two lectures shows that more is known about the physiology and pathology of diabetes mellitus than of any other disease. That this knowledge is, nevertheless, subject to important biochemical limitations is made clear from that section of Prof. H. S. RAPER'S address to the British Association for the Advancement of Science which deals with the hydrolysis and synthesis of glycogen in the human body (see p. 509). For example, it is not yet known how a synthetic product like glycogen is dealt with in the cell so as to protect it from the disruptive agencies which exist there. Arrangements for this purpose must be present since we know that substances may accumulate in cells which contain enzymes that hydrolyse them; for example, glycogen and amylase coexist in the liver cell. Again it has been proved that when glycogen breaks down in the liver it gives rise to glucose, and it is generally assumed that the synthesis of glycogen from glucose in the cell is brought about by the simple reversal of a hydrolysis which may be catalysed by enzymes under appropriate conditions. These conditions have, however, not yet been realised in vitro, and Prof. RAPER gives reasons for believing that the process is less simple. In his view it is probable that only the living cell can bring about the synthesis of glycogen. And it is at least possible that the substances from which glycogen is produced or bodies derived from them must first become bound up with, or at some stage form an integral part of, the living structure before they are converted into glycogen. Thus much remains to be learnt about even the main biochemical processes which control the metabolism of sugar in the animal body. But in spite of these gaps in our knowledge, the principles

[1] Quart. Jour. Med., 1929, xxii., 191.

of treatment of diabetes mellitus are beginning to stand out clearly, and it will be of interest to see how far these principles can be applied in the treatment of other diseases.

THE WINNIPEG MEETING.

FOR the third time in its life—it is now only two years short of a century—the British Medical Association has met in Canada, where it has been warmly received, the opening ceremony coinciding in fact with a rather embarrassing heat wave. The Toronto meeting of 1906 was held in a storm, during which one of the hospitals was struck by lightning. Of the Montreal meeting held nine years earlier, at which Lord LISTER laid the foundation-stone of the Jubilee Nurses' Home, we have no meteorological recollections. The third has been the largest, the number of registrations exceeding 2900, and the rendezvous all the more fitting inasmuch as the University of Manitoba and its College of Physicians and Surgeons, almost alone of the Canadian provinces, maintain full medical reciprocity with this country. The harassing restrictions of licensure were touched on in a moving part of Prof. HARVEY SMITH'S presidential address, which appeared in our columns last week. Our own General Medical Council has reiterated its desire for Imperial reciprocity of recognition in regard to medical qualifications, a reciprocity which would be facilitated if the Canadian provinces could come to some common agreement about their acceptance of the British Register. In addition to the presidential address, four important clinical addresses were given at Winnipeg. Sir LENTHAL CHEATLE dealt with the primary tumour in breast carcinoma on lines made familiar by his article in a recent issue of the *Cancer Review* (February, 1930). Sir WILLIAM WHEELER'S address on the significance of recoil following visceral decompression touched on the fringe of problems which concern not only surgeons but biochemists and physiologists. An abstract of this appears on page 541 of our present issue. Dr. W. E. DIXON'S address on drug addiction dealt in succession with the caffeine beverages, alcohol, heroin, cocaine, and the newest habit-forming drugs, and included an attempt to assess the world's need of narcotics in order to ensure that restriction shall inflict no hardship on the poor. The final address was on rest, work and play, in health and disease, by Sir FARQUHAR BUZZARD. His reminder that the recreation obtained from games depends mainly on the interest they evoke in the patient is timely; many practitioners nowadays forget that their own enthusiasm for athletic pursuits is not universally shared, and that some patients may prefer to earn by morning exercises the liberty to spend their days in more congenial occupations. On the last day of the meeting the Lister Oration was delivered by Lord MOYNIHAN, who commemorated JOSEPH LISTER in four aspects as benefactor, Quaker, surgeon, and man. The prevailing opinion, he said, was that LISTER was able to do what he did because of his supreme intellectual gifts. What was so often overlooked, he added, was LISTER'S possession of other qualities: his great heart, his humanity, his faith, his intellectual integrity. The clinical and scientific work of the meeting was organised in 14 sections, of which some account will be given in later issues. In the Section of Medicine the subjects of filtrable viruses, functional disorders of the colon, and acute poliomyelitis were covered in successive sessions; in the Section of Surgery, recent advances in thoracic surgery, the uses of radium in surgery, and the surgery of the sympathetic nervous system. Special importance attached to the meeting of the Section of Tuberculosis, as it coincided with a visit of the British tuberculosis experts who had been making a prolonged tour of the United States and Canada.

LONDON RUBBISH.

LONDON contains an unparalleled conglomeration of human beings, whose rubbish presents a vast and complex problem about which everyone is becoming anxious. It is agreed that the metropolis is far behind the times in its arrangements for the collection of household refuse, and that the disposal works are out of date and inefficient. Matters were brought to a head by the issue last year of a highly condemnatory report[1] by a Government official in which every class of the community came in for blame. Householders were scolded because they do not burn their refuse, although their ability to do so has been impaired by installing gas fires in accordance with the injunction not to make black smoke; the contractor was scolded for collecting refuse more cheaply than the local sanitary authority is able to do; the authorities were scolded for not adopting uniform methods, although there is no agreement as to what method is the best. The Departmental Committee which was appointed to consider the Dawes report has now issued its recommendations,[2] of which the first and most important are:

(1) That it is no longer practicable for the 29 Metropolitan Sanitary Authorities within the highly developed area of the Administrative County of London separately to dispose of their refuse efficiently, economically and without causing a nuisance, and that the disposal of house, trade and street refuse in London should be centralised and placed under the control of one body.

(2) That the central body should also be responsible for the general coördination of the public cleansing service of London so as to secure, to the fullest possible extent, such uniformity of organisation and equipment as would facilitate the work in all its branches, and that it should therefore have jurisdiction over (*a*) types of refuse collection vehicles and refuse receptacles; (*b*) frequency of refuse collection; (*c*) inflow of refuse to discharge points; (*d*) avoidance of anomalies arising out of borough boundaries; (*e*) types of street cleansing vehicles and general equipment.

The formation and success of the Metropolitan Water Board has evidently led to the suggestion that there should be a Metropolitan Refuse

[1] See THE LANCET, 1929, i., 781.

[2] Ministry of Health. Report of the Departmental Committee on London Cleansing. Cmd. 3613. H.M. Stationery Office. Pp. 27. 6*d*.

Disposal Board; but there is a considerable body of informed opinion which finds little parallel between the problems presented by the supply of water and the collection and disposal of refuse, and which is distrustful of over-organisation. What are the leading facts? Admittedly there is a lack of uniformity in the methods of collecting the material, the arrangements for disposal of the refuse are in the hands of a few contractors among whom there is little or no effective competition, and the dumping of refuse—not only from London but from the great towns in the Outer Ring—in the country and semi-country round about the metropolis has caused much heart-burning. Dumps on the Essex marshes and elsewhere caught fire, emitted poignant smoke, served as a breeding place for flies and rats, and, owing to the continued extension of building, became an offence to an increasing number of persons. Administrative action was taken meanwhile in regard to a number of these dumps, the situation being improved by changed methods in depositing and covering the refuse. Miss SUSAN LAWRENCE, while describing the Essex dumps as a public scandal, pointed out that no Essex authority had yet made full use of its existing powers under the Public Health Act, and stated that the Ministry of Health would press for the discontinuance of insanitary dumps. Her remarks seemed to exclude the prospect of further legislation in the near future.

The Departmental Committee was not itself united on the constitution of the suggested central authority. Two members did not see their way to recommend the setting up of a new body with independent control, as this would involve interference with the powers of existing sanitary authorities. There is no reason to believe that most if not all of these authorities would not bring valuable contributions to a conference with the Ministry of Health on the collection and disposal of rubbish, or that they would not fall in with any suggestion made to them. The recent discussion at the Society of Medical Officers of Health made this pretty clear. No evidence was laid before the Committee that cleansing can be more efficiently done on a larger than on a smaller scale; no new methods were suggested that are not already well known to the cleansing departments. Dumping must be continued because there is ground to be levelled; salvage is of dubious value, although no objection can be raised to the use of suitable household refuse for brick-making provided the refuse is stored in an isolated situation; there is no consensus of opinion that electricity can be produced economically by burning refuse in destructors, even on a large scale. But now that public interest has been aroused, it may well be hoped that sufficient money will be spent on modern equipment for dust collection and for its hygienic disposal, use being made of the machinery of government available to-day.

ANNOTATIONS

VITAL STATISTICS FOR 1929.

The Registrar-General's Statistical Review for the year 1929, Part I. of which has just appeared,[1] confirms the provisional figures for the general birth-rate, death-rate, and infantile mortality issued earlier in the year.[2] The birth-rate of 16·3 per 1000 persons living at all ages was the lowest recorded since the establishment of civil registration in this country, the lowest rates previously being 16·6 for 1927 and 16·7 for 1928. The death-rate of 13·4 per 1000, against 11·7 for the previous year, was the highest since 1919, the increase being due almost entirely to the high mortality from respiratory and circulatory diseases and to the epidemic of influenza during the severe cold of February and March. The infantile mortality-rate of 74 per 1000 live births was 9 per 1000 above that of the previous year, the excess again due to the high mortality of the first quarter. With the exception of the pandemic of 1918–19 the epidemic of influenza was the most severe experienced in this country since the disease reappeared in 1890–91, the mortality being equal to 734 per million living against 196 in 1928. The mortality from respiratory diseases rose from 1507 in 1928 to 2104 per million, but the latter figure had been exceeded in 1920, 1922, and 1924. The mortality from circulatory diseases reached the record figure of 3030 per million, due largely to the deaths of elderly persons during the cold weather of the first quarter of the year. The death-rate from cancer was 1437 per million living against 1425 for the previous year, thus continuing the steady though slight increase over all recent years and being the highest crude rate recorded. The increase affected both sexes but was rather greater for females than for males. The mortality of women from puerperal sepsis and accidents of pregnancy and childbirth was 4·33 per 1000 live births, compared with 4·42 in the previous year. The improvement was not in respect of puerperal sepsis, which actually increased from 1·79 to 1·80, but in "other accidents of pregnancy and childbirth" which improved from 2·63 to 2·53. Although lower than that in 1928 the combined rate is still above the experience of the seven years 1921–27.

[1] H.M. Stationery Office. 7*s*. 6*d*.
[2] See THE LANCET, 1930, i., 195.

OPIUM AND SCOPOLAMINE BY THE MOUTH IN OBSTETRICS.

IN a long article, which is too largely composed of special pleading of a sentimental nature, H. Selheim discusses the pros and cons of the use of anæsthetics in midwifery.[1] With most of his opinions most English obstetricians are, no doubt, in agreement, for they express the general desire to reduce any intense pain in labour or so to control the natural process as to make it as little painful and as little dangerous as possible to the mother as well as the child. When it comes to practical recommendations for bringing about this desired end the novel suggestion offered by Selheim is that midwives should be allowed to administer omnopon and scopolamine by the mouth at the doctor's orders. He recommends a

[1] Med. Klinik, 1930, xxvi., 1103.

particular preparation for use in private practice consisting of omnopon 0·015 g., scopolamine hydrobrom. 0·0005 g., dissolved in brandy and syrup. The dose is to be given about three-quarters of an hour before the most painful stage of labour is anticipated. It may well be that some provision of this kind will be the essential outcome of the desire in this country to bring a measure of alleviation to the labour pains of the thousands of mothers who are confined outside institutions and under conditions which do not permit of ordinary anæsthetic administration.

CONGENITAL CLUB-FOOT.

In 1928 the British Orthopædic Association chose club-foot for the subject of the Robert Jones Gold Medal. The selection of this deformity for a prize essay was timely, for no comprehensive description of its pathology and its treatment seems to have been attempted in English since William Adams published his Jacksonian monograph on the same subject in 1873. Mr. E. P. Brockman, who has now published in the form of a monograph[1] the essay which earned him the medal, begins with an historical survey of the subject; this chapter provides a fair outline of the progress of orthopædic surgery, since the history of the treatment of club-foot up to the advent of Listerian surgery is really a reflection of the evolution of orthopædics. In discussing the nature of the deformity, Mr. Brockman describes the foot as being adducted, inverted, in equinus, and, lastly, plantar flexed or plantaris; this last term was originally introduced by F. R. Fisher, and is here revived with good effect. A suggestive analogy is drawn between club-foot and congenital dislocation of the hip. Mr. Brockman brings forward strong evidence, both clinical and pathological, for maintaining that club-foot is really a dislocation of the astragalo-scapho-calcanean joint, but that the astragalus is practically stationary, whereas the scaphoid has moved downwards, backwards, and inwards, carrying the forepart of the foot with it; the os calcis has also moved inwards. The effect of this migration is to approximate the scaphoid to the sustentaculum tali and thereby to diminish the natural capacity of the socket for the head of the astragalus, which consequently slips out uncovered and becomes palpable on the dorsum of the foot. From this view of the nature of the deformity the author passes on to a full discussion of its ætiology; the various theories are passed under review, a preference being expressed for the hypothesis that the deformity is due to an irregular development of the tissues of the foot and that the fault is of intrinsic origin and independent of extrafœtal influences. This view, it is maintained, best fits the pathological findings; the bones are least affected, for they are of normal shape, but the calcaneo-scaphoid ligaments may be deficient or absent and the muscles which control the socket for the head of the astragalus are contracted. The treatment of club-foot is well described and the difficulties associated with the unfolding of the deformity are thoroughly considered and discussed.

The ideal time to start treatment is about 10 days after birth; the necessary manipulations are set out in detail and the method of splinting favoured is that by means of strapping. The author deprecates the enlistment of the mother to participate in giving treatment, because of the force necessary in handling the foot, but some surgeons would not agree with this view. An intelligent mother is quite capable of carrying out the initial graduated manipulations, massage, and splintage. Tendon tenotomy, which at one time was so popular, is now used only when a resistant equinus remains, to cure which the tendo Achillis may be cut. But the plantar fascia often needs subcutaneous section as an aid to manipulation. In older children manipulation under anæsthesia with plaster-of-Paris fixation is the best procedure, but quite a number of patients are incompletely corrected by this means, and for them open operation is advocated after the age of 3 years. The type of operation described is in principle the one practised in recent years by orthopædic surgeons in this country; the author adds one or two modifications of his own. Ligaments and muscles only are cut, the bones are untouched. The plantar fascia and muscles are detached as far backwards and inwards as possible; the tibialis posticus is exposed and if very contracted is detached from the scaphoid and other tarsal bones. The scapho-calcanean joint is next identified and the ligaments on its inner and inferior aspect incised. By manipulating the foot the deformity should now be capable of correction and can be maintained in the proper position by plaster-of-Paris. In the after-care the teaching of corrective exercises to the child is important. But there remains the stubborn foot, familiar to all orthopædic surgeons of experience, for correction of which none of the procedures named is effective. For this intractable condition a bone operation is necessary, but we agree with Mr. Brockman that this should be delayed until near puberty. Each surgeon has his own method of attack on each case, for standardised plans are of little avail in the major degrees of deformity. Mr. Brockman favours Dunn's operation, which consists of an excision of the scaphoid and arthrodesis of the astragalo-calcanean, the calcaneo-cupoid, and the astragalo-cuneiform joints. Mr. Brockman has provided clear, well-reasoned teaching on one of the most baffling deformities which surgeons are called upon to treat.

[1] Congenital Club-Foot (talipes equinovarus). By E. P. Brockman, M.Chir., F.R.C.S., Orthopædic Surgeon, Westminster Hospital; Assistant Surgeon, the Royal National Orthopædic Hospital. Bristol: John Wright and Sons, Ltd. 1930. Pp. 110. 10*s.* 6*d.*

SMALL-POX AND VACCINATION.

The July *Bulletin* of the Office International d'Hygiène Publique in Paris includes a supplement[1] which will be found valuable by all those who are concerned with the control of small-pox and the promotion of vaccination. The supplement consists of an interim report of the Commission on small-pox and vaccination which was made to, and accepted by, the Permanent Committee of the International Health Office at its last session in May. The Commission dealt in this report with three questions: (1) nomenclature of the varieties of small-pox; (2) the occurrence and distribution of post-vaccinal encephalitis; and (3) the methods of vaccination and the dosage of vaccine which are officialy enjoined in different countries of the world. In so doing, the Commission has touched upon matters which are, at the present time, of special interest in England, and recent English experience has been freely drawn upon. The Commission has carried a stage further the decision of the International Conference on the Nomenclature of Causes of Death, 1929, that the generic term *variola* should be recognised as comprising at least two varieties, *variola major* and *variola*

[1] Obtainable from the Office International, 195, Boulevard St. Germain, Paris.

minor, or alastrim. The distinction, it is emphasised, is one of epidemiological type rather than of mere clinical characteristics of the individual case. Those whose function it is to collect data as to the occurrence of severe complications and deaths, particularly among the unvaccinated at the most susceptible ages, are usually in a position to satisfy themselves, in the course of an epidemic, that the prevalent disease is of the "minor" variety, with few complications and practically no mortality, or that it is the "major" or Eastern type of small-pox, and can apply administrative measures in the light of this knowledge, always with the confidence that the well vaccinated are protected against any variety of small-pox. In respect of post-vaccinal encephalitis, the Commission has been fortunate in being able to collate the experience of two countries in which this rare complication has been most conspicuous—England and Holland. It has found that the same complication is liable to occur after the use of many different strains of lymph in other countries in Europe, and that it must be regarded as a definite risk associated with vaccination, although it is one which is so rare as hardly to require consideration unless the vaccination practice of the country entails the extensive primary vaccination of children at school ages, when it is undoubtedly a factor which has to be reckoned with. In this respect the Commission follows closely the findings of the report of Sir H. Rolleston's Vaccination Committee in 1928. The last part of the Commission's report gives an instructive epitome of the different ways in which vaccination is practised in different countries, and presents a summary of replies to a detailed questionaire which the Office International d'Hygiène Publique addressed last year to the several Governments which it represents. Most of the data given and the opinions expressed in this report are new only in the sense that they have been brought together in a convenient form from many parts of the world, but they derive special value from the broad basis of the inquiry, and from the authority given to them by the representatives of the numerous national public health services who took part in it.

THE COLOUR IN JAUNDICE.

THE usual complexion of the patient influences very greatly the colour of his jaundice; those who are pale and fair tend to present a bright lemon-yellow colour, but if the patient is naturally dark the colour is more of an orange tint or bronze. If associated cyanosis is present from other causes, a peculiar olive hue is produced; a similar green jaundice may occur without cyanosis, and it was long thought that such cases were especially unpromising ones. An interesting analysis of jaundice by Prof. T. Brugsch[1] is a welcome combination of clinical observation and laboratory investigation. He suggests a division of cases of jaundice according to their colour into four types, a "red," a "green," a "flavin," and a "melasikterus," the last being that browny tint which Brugsch compares in the name "melasikterus" to the colour of treacle or molasses. According to him frank green jaundice is only found with mechanically produced icterus—that is, some obstruction is present leading to biliary stasis, concentration of the bile, and absorption of this "thickened" bile into the blood; the tint is due to discoloration of the skin with biliverdin. Red jaundice, on the other hand, occurs in all "hepatotoxic" types, such as acute and subacute liver atrophy, and is due to the presence of bilirubin in the skin. The former colour is thus associated with biliary retention, the latter with failure of biliary secretion. When obstruction is present the bile retained in the biliary passages is for the most part oxidised to biliverdin, so that the more such oxidation takes place the greener becomes the jaundice; for this reason the direct reaction of the van den Bergh test in the blood-serum may gradually disappear and its place be taken by an indirect reaction, although the jaundice is undoubtedly obstructive in origin. In red jaundice no oxidation of bilirubin to biliverdin occurs, since the body tissues, apart from the biliary tract, do not appear to possess this property of oxidation; thus any appearance of biliverdin in tissues, skin, or urine is an indication of biliary stagnation. Flavin icterus Brugsch defines as that yellow jaundice which occurs with an indirect van den Bergh reaction in such conditions as hæmolytic jaundice, anæmia gravis, icterus neonatorum, and splenic anæmia. It is jaundice produced outside the liver and especially concerned with the reticulo-endothelial system, particularly the spleen. Clinically the colour is lighter than the red jaundice though of similar tint. Melasikterus is the type seen in conditions of cachexia and is rather a brown pigmentation than a true icterus. The differentiation of these clinical types of jaundice may be further assisted by a study of the iron in the skin. In the presence of the ferric ion an intradermal injection of potassium ferricyanide (freshly prepared 1 per cent. solution) produces a blue colour which is quite independent of the bile-pigments themselves. A positive iron reaction in the skin thus shows the presence therein of bivalent iron and together with a true bilirubin jaundice indicates an origin from hæmoglobin breakdown. It is thus positive in red (hepatotoxic) jaundice and negative in green (obstructive) jaundice. It suggests a disorder of the liver-cells themselves.

It must be admitted that the exact mechanism of some types of jaundice is still far from clear, and in particular the rôle of the iron molecule is perhaps not as simple as might be believed from Prof. Brugsch's account. At the same time the broad divisions of colour described in his paper are interesting and serve to emphasise the importance of bedside observation.

LABORATORY OUTBREAKS OF PSITTACOSIS.

RECENT investigations of psittacosis in America have had dramatic sequelæ. In many of the laboratories where the disease has been studied cases of infection amongst research workers and attendants have occurred, some of which have proved fatal. Investigators at first assumed that psittacosis was an *aertrycke* or allied infection, and adopted what they considered suitable precautions, only to find that these were quite inadequate. But even those who came later on the scene, and were forewarned by the bitter experience of their predecessors, have not escaped, for one case of infection has occurred at the Rockefeller Institute despite most elaborate precautions. Perhaps none of these outbreaks has been quite so remarkable as that occurring in the Public Health Laboratories, Washington, which provided the material for a clinical survey by E. Petersen, O. B. Spalding, and O. Wildman.[1] This outbreak affected 11 persons; but its magnitude is not its most important feature, for of these 11 persons 9 had no access to the rooms in which the psittacosis investigation was being carried out. The laboratories concerned are housed in three

[1] Zur Analyse des Ikterus, Med. Klin., 1930, xxv., 413.

[1] Jour. Amer. Med. Assoc., 1930, xcv., 171.

buildings which communicate by tunnels and causeways, but the 11 cases of infection were confined to the personnel of the building in which the psittacosis investigations were being pursued and did not spread into the two other buildings. The infected birds were received on Jan. 16th, and of the three workers who handled them two fell ill on Jan. 25th and Feb. 6th respectively; one case proved fatal. The remaining nine cases appeared on Feb. 15th, 28th, March 10th, 11th, 12th, 13th (two cases) 14th, and 15th. It will be observed that the last seven cases occurred close together, suggesting, as G. W. McCoy points out[2] that they became infected about the same time from a common source. The nature of this common source of infection is obscure. Had any of the patients infected others in their homes one might have thought that the laboratory outbreak was due to spread from man to man; but no home infections occurred and, moreover, the history of this disease suggests that the human case is a negligible source of infection. Why infections should spread from parrot to man with such ease and from man to man with such difficulty remains a mystery, but an almost identical problem is presented by tularæmia and a most interesting line of research awaits the intrepid investigator of either of these infections. We have been fortunate in this country for, with precautions certainly no more elaborate than those adopted elsewhere, laboratory infections have not occurred apart from one relatively mild case.

The clinical part of Petersen, Spalding, and Wildman's communication covers ground now well known and brings no new facts to light. In his investigation of this disease in the Argentine last year E. Barros[3] made free use of X ray examination of the chest and spoke highly of its value. And if convalescent serum has not been used in this country in the treatment of psittacosis, it is for the good reason that experiment has shown it to have little or no protective value.[4] This finding is supported by the results now reported, for in our opinion the evidence provided contains no justification for the conclusion that the use of immune serum in daily doses was of "apparent benefit." A. P. Thomson obtained comparable results with serum from individuals recently inoculated with T.A.B. vaccine.

"SOCIAL ORTHOPÆDICS."

SINCE 1924 the *Cripples' Journal* and the *Cripple* have served a useful purpose in keeping the social side of work for physically disabled children before a wide public, and before these journals came to an end (at all events in their present form) their editor, Mr. Frederick Watson, called on the expert knowledge of his collaborators to produce a book[5] which he describes as "nothing more ambitious than an outline of some past and future problems of disablement in domestic life and industry." He does less than justice to an enthralling account of the fate of the cripple through the ages, from the Old Testament conception of deformity as a thing accurst, and the persecution of the Middle Ages, to the belated humanitarianism of the nineteenth century. In this historical survey he touches on the deformities once common among lace-making children in England, one of the evils of child labour which is still vigorously alive among the carpet-makers in Persia. A chapter on the influence of the war shows the evolution of the voluntary county and after-care clinics in Shropshire, as a result of the stimulation of public sympathy towards crippling; following this came the Red Cross campaign against rheumatism. In discussing the education and training of the cripple Mr. Watson stresses the importance to the State of a man who can bear at least part of the burden of his maintenance. In this field America has far out-distanced us; an interesting chapter is devoted to the American scheme, under which every citizen has a right to vocational training for direct employment or rehabilitation after accidental injury. In the final chapter is outlined an abstract rather than a concrete constructive policy, but at the present time it is perhaps impossible to do more. In the establishment of the new faith of humanitarianism and in the extension of voluntary agencies for their relief and education cripples will, he believes, find salvation. The book is appropriately dedicated to Sir Robert Jones.

[2] U.S. Public Health Reports, 1930, xlv., 843.
[3] Dia Médico, Dec. 30th, 1929.
[4] Sacquépée, E., and Ferrabouc, L.: Presse Méd., 1930, xxxviii., 569, and London Hospital Investigations (unpublished).
[5] Civilisation and the Cripple. London: John Bale, Sons and Danielsson. 1930. Pp. 120. 10*s.* 6*d.*

THE TREATMENT OF TETANUS.

THE treatment of tetanus by massive doses of antitoxin has a sound basis of experimental work. In 1917 Sherrington showed that antitoxin injected in suitable amounts would protect monkeys in which the disease had been produced artificially by the injection of toxin, but attempts to cure patients already showing signs of infection by this means have proved disappointing. Dr. A. E. Paterson[1] has just published the results of treatment of tetanus in children by larger doses of antitoxin than have previously been given. These results are so strikingly successful in comparison with those of previous observers that his method deserves wide publicity. The outstanding feature of his practice is the amount of antitoxin given both at the beginning and throughout the illness. As a routine 100,000 (American) units are given intravenously and 40,000 intramuscularly in the first place; the former dose is repeated in 12 hours and then again at 24-hourly intervals according to the clinical progress of the case, while the latter is repeated four-hourly, the amounts being gradually lessened and later given at less frequent intervals. With this method of 26 consecutive patients 19 recovered, the dosage in the successful cases ranging from 120,000 to 1,970,000 units. Difficulties connected with this treatment are that intravenous therapy in patients with tetanus, especially in children, usually requires a general anæsthetic, and the expense of large doses of antitoxin is considerable. Moreover, the injection of a large amount of horse serum is not easy. The last-named obstacle has happily been considerably mitigated by the more concentrated antitoxin now on the market, the volume of 100,000 units now being 60 to 70 c.cm. instead of 300 c.cm. as formerly. Dr. Paterson quotes some cases in his series which are of especial interest. One patient with an incubation period of six days progressed well for five days but then died suddenly during a spasm. He had only been given 240,000 units of antitoxin in this time, and it is possible, in view of the results with later cases, that larger doses might have saved his life. Another case showed clearly that antitoxin should not be discontinued too soon, but should be carried on well into convalescence. This was a moderately severe infection which reacted well during the first few days of treatment. The intravenous injections were,

[1] Med. Jour. of Australia. 1930, i., 832.

therefore, discontinued during the fourth day, but on the fifth day the patient relapsed and the dose had to be increased again. The patient then recovered. Topley and Wilson [2] explain the discrepancy between Sherrington's results and those obtained in clinical practice by the facts that toxin and not bacilli were injected by him and that the doses he used were enormous considering the weight of the animals. The dosage used by Dr. Paterson is relatively only slightly less than that used by Sherrington. The author is the first to admit that his series is too small for any certain claims about the value of massive doses of antitoxin to be made. They do, however, strongly indicate that the doses used hitherto have been much too small, and his results justify an extensive trial of larger doses particularly now that concentration of serum has overcome one of the chief technical difficulties.

INCIDENCE OF CANCER IN MENTAL PATIENTS.

RELATIVE immunity to cancer in races and individuals is always of interest and the detailed investigation of the phenomenon has been considered a fruitful path of research. The incidence of cancer on certain races in Europe was studied in 1925 for the League of Nations Subcommittee on cancer statistics, and Prof. Eugène Pittard, after undertaking this investigation, had little doubt that the Nordic race was more subject to cancer than the other European races and the Mediterranean race least so. A less complex problem for detailed research was suggested by the Commissioners for Lunacy in England, who in their annual report for 1909 made the observation that the asylum patient appeared to be relatively immune to cancer, as also to bronchitis, compared with the general population. The Commissioners pointed out that the age incidence was the same in the two groups—that is to say, the normal population and the mentally affected, and that there had been the same apparent increase in the incidence of cancer in both sections of the community in recent years. Although the subject came under notice again in 1923, nothing was done till 1929 when the newly created infectious diseases subcommittee of the Royal Medico-Psychological Association sent round a questionaire to 72 mental hospitals and then referred the replies to a professional statistician. The outcome[3] shows, first, that both in the sane and the insane there has been a steady increase in the mortality from cancer recorded during the last 10 years from 1919–29. Whether this is a real increase or merely an apparent one due to more accurate statistics it is impossible to say; since medical statistics were quite inadequate in the past, an increase in cancer cases with more carefully compiled figures is to be expected. Secondly, the figures show that approximately one-seventh of the deaths in England and Wales are attributable to cancer whereas only one-twenty-sixth of the deaths in the mental hospitals are due to this disease—a much lower figure. Finally, for the period 1920–28 the death-rates from all causes in the 72 mental hospitals are compared with those among persons aged 15 years and upwards in the general population of England and Wales. The total death-rates are 79 in the mental hospitals and 13 in the general population, while a comparison of cancer death-rates show that there are 306 in the mental hospitals to 176 in the general population—i.e., less than twice as high. Before accepting these figures as representative it is necessary to ascertain how far the lower proportion of deaths from cancer in the mental hospitals is explainable by the very heavy death-rates in these institutions from other causes, such as general paralysis and tuberculosis. The "professional statistician" (unnamed) who analysed the figures for the Association draws attention to this need, and it is to be hoped that this important part of the study will receive prompt attention. Meanwhile an interesting addition to the report is the outcome of an investigation carried out by Dr. Arthur Pool at the County Mental Hospital, Rainhill. Dr. Pool undertook a study of the incidence of cancer in this institution over a period of 25 years, basing his figures upon an analysis of post-mortem records. He believes his results to confirm the low incidence of cancer in mental hospitals compared with the general community, but finds no increase in incidence with the passage of years; this last result, based as it is on actual port-mortem findings, is worthy of consideration. It is not, however, recorded what proportion of patients dying in the institution during the period covered by the inquiry were submitted to autopsy. If this proportion was not very high indeed some cases of cancer may have been missed. This is a less unwieldly field of research than is presented by the investigation of racial cancer; but more work, will be necessary to eliminate possible errors before definite conclusions can be drawn on the lines of detailed research planned out.

[2] Principles of Bacteriology and Immunity, London, 1930.

[3] (*a*) First Report on the Comparative Incidence of Cancer in Mental Hospital Patients and in the General Population of England. By J. R. Lord, C.B.E., M.D., F.R.C.P. Edin., and M. J. McGrath, M.B., D.P.M. (*b*) The Incidence of Cancer at Rainhill Mental Hospital. By Arthur Pool, M.D., M.R.C.P., D.P.M. London: Adlard and Son. 1930. Pp. 22. 9*d*.

INTERNATIONAL LEAGUE AGAINST TRACHOMA.

IT is proposed that the next meeting of this League should be held in June, 1931, at Budapest. At the recent meeting of the League at Geneva, when Prof. de Grosz was elected President, the following were chosen as vice-presidents and members of the executive committee: Dr. Marquez (who was chairman of the International Ophthalmological Congress in Madrid), Mr. Szymansky (President of the Polish Upper House), Mr. MacCallan (representing the Ophthalmological Society of the United Kingdom), Mr. Morax (Paris), Mr. Angelucci (Naples), Mr. Birch-Hirschfeld (Königsberg). Other members of the executive committee are Mr. Brandes (Antwerp), Mr. Kadlicky (Prague), Mr. van der Hoeve (Leiden), Mr. de Lapersonne (Paris), Mr. Park Lewis (Buffalo, U.S.A.), and Mr. Miyashita (Tokyo).

THE ORAL ADMINISTRATION OF ŒSTRIN.

To the lay and also many medical minds it must have caused some astonishment that the International Congress for Sex Research, held in London during August, was concerned less with the sociological aspect than with the chemical side of sexual activity. The papers and discussions for the most part centred round the physical, chemical, and physiological properties of the internal secretions of the sex glands. It has long been known that the glands of internal secretion which play a part in sexual functions are not merely the gonads themselves but include more particularly the pituitary. In fact, recent work has been concentrated on the pituitary and the placenta to such an extent that œstrin and the testicular hormones have been temporarily eclipsed. Many of the communications at the Congress emphasised the importance of the pituitary, but the gonads were given due prominence. At Chicago, T. F. Gallagher,

F. C. Koch, and their colleagues have been working on the testicular hormone and described, among other developments, the method of testing the extract of testes upon comb growth in capons. The properties of the hormone were detailed. It seems clear that this work opened up an entirely new field in endocrine work. Amongst a number of interesting communications was one by Schoeller, Dohrn, and Hohlweg which dealt with the vexed question whether œstrin is active when given by the mouth. The original workers in America hold definitely that œstrin is inactive when given in this way, but in Europe it has been shown that oral administration can be effective under certain conditions. Allan, Dickens, and Dodds [1] found that some 25–30 times the subcutaneous dose was necessary to produce an effect on rats and that the distribution of the dose played a very important part in determining its activity by the oral as well as by the subcutaneous route. In Germany it has been claimed by many of the foremost workers that the amount required to produce œstrus when given by mouth is relatively little greater than when the subcutaneous route is employed; thus, Zondek maintains that the relationship is 5 : 1. Laqueur, on the other hand, maintains that 100 times the subcutaneous dose is necessary to produce signs of activity. Schoeller, Dohrn, and Hohlweg have now proved that another factor besides the distribution of the dose is significant—i.e., the purity of the material used by the different workers. Experiments with material of different degrees of purity showed the less pure material to have the stronger effect. Thus, with the pure crystallised follicular hormone (8 million units per gramme), it required 50 rat units to produce œstrus in 50 per cent. of the animals; with a preparation containing one million units per gramme 30 rat units were sufficient, and with one containing 0·2 million units per gramme 6 rat units had the desired effect. Moreover, it was found that with the aqueous alcoholic preparations the potency increased approximately in proportion to the amount of alcohol added. These important observations open afresh the question of giving hormones by the mouth, and it may be that a careful preparation of œstrin will be found effective when given orally.

[1] Jour. Physiol., 1930, lxviii., 348.

STATISTICS OF MEDICAL PROFESSION IN GERMANY.—A statistical record of the German Health Office states that the number of medical men has increased between 1887 and 1928 from 15,824 to 43,948. In 1887 7·2 medical men existed for each 10,000 of the population, whilst in 1928 33 were registered, that is, while there was formerly one medical man to 3000, now there is one to only 1400 inhabitants. From 1909, when qualifications were first granted to women, to 1913, the proportion of medical women to medical men was 1 : 26·5 against 1 : 5·4 in 1928. In 1928 the number of specialists was 8000, of whom 188 were medical women; 63 per cent. of the profession lived in towns and 37 per cent. in the country, the respective number for women being 79 and 21 per cent. respectively. While the number of medical men and women is continually on the increase, the number of midwives is diminishing. The number of nurses with general training is also increasing, the records for 1887 and 1928 being 14,000 and 102,000 respectively. As to unqualified persons, there were 1713 in 1887 against 12,000 in 1928, so that for each 10 qualified medical men and women 2·64 quacks are now engaged in practice.

THE SERVICES

ROYAL NAVAL MEDICAL SERVICE.

Proby. Surg. Lt. J. J. Dwyer to be Surg. Lt.

Surg. Lts. C. H. Birt to *Ormonde* and R. E. P. Cohen to *Glorious*.

ROYAL NAVAL VOLUNTEER RESERVE.

Surg. Lt.-Comdr. G. A. Clark to *Victory*, for R.N. Hospital, Haslar.

Surg. Lt. A. S. Bradlaw to be Surg. Lt.-Comdr.

Surg. Lt. (D.) C. H. A. Fido to be Surg. Lt.-Comdr. (D.).

Surg. Sub-Lts. J. N. Matthews to *Champion* and B. Blewitt to *Victory*, for R.N. Hospital, Haslar.

Prob. Surg. Lt. (D.) H. P. Buchanan to *Victory*, for R.N. Hospital, Haslar.

Proby. Surg. Sub-Lts. J. C. Moor and J. E. Davenport to be Surg. Sub-Lts.

ROYAL ARMY MEDICAL CORPS.

The undermentioned Majs. (temp. Lt.-Cols.) to be Lt.-Cols.: E. Gibbon, vice Lt.-Col. T. S. Coates, promoted, and R. W. D. Leslie, vice Lt.-Col. M. G. Winder, retd.

The undermentioned Majs. to be temp. Lt.-Cols.: C. Scaife and D. M. Corbett.

Capt. D. C. Bowie to be Maj. (prov.).

The undermentioned Lts. to be Capts. (prov.): T. E. Moles and J. H. Anderson.

Lt.-Col. E. W. Siberry, having attained the age-limit of liability to recall, ceases to belong to the Res. of Off.

Lt.-Col. M. G. Winder retires on retd. pay.

Lt. E. H. Hall to be Capt. (prov.) and remains secd.

The undermentioned Lts. (on prob.) are secd. under the provisions of Art. 205, Royal Warrant for Pay and Promotion, 1926: J. T. Robinson, T. M. Corcoran, and R. L. Whittaker.

The undermentioned Lts. (on prob.) are confirmed in their rank: H. C. Benson, D. A'Brook, A. N. B. Odbert, W. J. Officer, T. N. Fogarty, A. F. Kennedy, and J. C. Macfarlane.

The undermentioned to be Lts. (on prob.): A. Guirdham, J. T. Robinson, M. A. Rea, and T. M. Corcoran.

Lt. F. R. Gedye resigns his commn.

ARMY DENTAL CORPS.

The undermentioned Capts. to be Majs.: C. T. Hastings, J. J. Boyle, and J. H. W. Fitzgerald.

Lt. (on prob.) A. F. D. Shapland is confirmed in his rank.

Maj. T. K. Place is placed on the half-pay list on account of ill-health.

ARMY RESERVE OF OFFICERS.

Lt.-Col. A. D. O'Carroll to be Lt.-Col.

Capt. G. Moore, having attained the age-limit, retires and retains his rank with permission to wear the prescribed uniform.

T. A. Danby to be Lt.

TERRITORIAL ARMY.

Capt. T. S. Goodwin to be Maj.

INDIAN MEDICAL SERVICE.

Capts. R. C. Watts and Hari Das to be Majors.

The undermentioned Capts. (prov.) are confirmed in their rank: C. A. Bozman, M. L. Ahuja, and W. J. L. Neal.

Lt. T. C. Puri to be Capt. (prov.).

Lt. (on prob.) A. K. M. Khan to be Capt. (prov.) (on prob.).

Lt. G. D. Mehta relinquishes his temp. commn.

INDIAN MEDICAL DEPARTMENT.

Senr. Asst. Surg. and Maj. A. E. Clarke retires.

ROYAL AIR FORCE.

E. W. B. Griffiths is granted a short service commission as a Flying Officer for three years on the Active List.

M. Pearson is granted a temporary commission as a Flying Officer.

Flight Lt. C. W. Coffey is transferred to the Reserve, Class D. (ii.).

Flight Lt. P. E. Brown is promoted to the rank of Squadron Leader on promotion to Maj. in the Army Dental Corps.

MACKENZIE MEDAL FOR OPHTHALMOLOGY.—The custodians of the Glasgow Eye Infirmary have awarded the William Mackenzie Medal for 1929 for original contributions to ophthalmology to Prof. J. van der Hoeve, of Leiden, Holland. At 8.30 P.M. on Oct. 3rd he will give an address at the Infirmary on Ophthalmology in its Relation to Other Branches of Medical Science.

CLINICAL INTERPRETATION OF AIDS TO DIAGNOSIS

A Series of Special Articles, contributed by invitation.

LXXXIII.

THE CLINICAL SIGNIFICANCE OF SLIT-LAMP APPEARANCES.

PART III.*

The Lens.

THE application of the slit-lamp to the crystalline lens has added to our knowledge of the anatomical and pathological appearances of this structure and the apparatus has become an essential for the diagnosis of various forms of cataract. Various means of examination are open to us:—

(*a*) Oblique illumination in focal light.
(*b*) Transillumination of anterior layers of lens substance by light reflected by deeper layers.
(*c*) Examination in zones of specular reflection, especially when viewing the anterior and posterior surfaces of the lens or those of the adult nucleus.
(*d*) Most important is the use of the optical section which aids us in judging the relative position of opacities and the approximate date of their appearance.

When the normal lens is examined it will at once be appreciated that it is not of uniform density throughout. It will also be observed that, in the adult lens at any rate, the changes in density occur somewhat abruptly so that various well-defined layers are brought into prominence.

The diagram (Fig. 6), taken from Koby's book, shows the various surfaces of discontinuity where these abrupt changes take place.

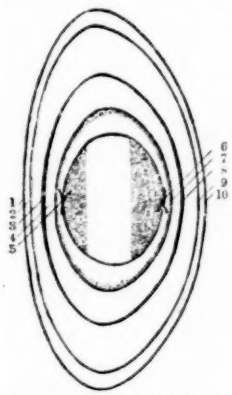

FIG. 6.—Diagram to show the surfaces of discontinuity of the lens. The numbers refer to the text. (Koby).

These so-called zones of discontinuity are named: (1) anterior band of the lens; (2) anterior band of discontinuity; (3) anterior band of the adult nucleus; (4) anterior peripheral band of the fœtal nucleus; (5) anterior central band of the fœtal nucleus; (6) posterior central band of the fœtal nucleus; (7) posterior peripheral band of the fœtal nucleus; (8) posterior band of the adult nucleus; (9) posterior band of disjunction; (10) posterior band of the lens. The clear interval between 5 and 6 is spoken of as the *central interval* of the fœtal nucleus, and here the density of the lens is most uniform. That portion of the lens between the anterior and posterior bands of the fœtal nucleus represents the lens at birth. By about 25 years the adult nucleus is completed, and that part of the lens which is outside these limits is called the cortex. The surfaces of the lens itself and those of the adult nucleus may be examined in the zone of specular reflection so that now we no longer merely examine images formed at these surfaces (the images of Purkinjé) but the surfaces themselves. It has long been known that there is a system of sutures at the surface of the lens, and the slit-lamp has shown that this system is present at the level of each surface of discontinuity. The sutures are simplest at the surfaces of the fœtal nucleus, the anterior being in the form of a Y, whilst the posterior is in the form of an inverted Y. These two figures are most useful in deciding the limits of the fœtal nucleus and hence in deciding the relative position of an opacity in the lens. The further removed we are from the surfaces of the nucleus the more complicated the suturing becomes. The surfaces of the adult nucleus in later life show a relief like a plastic geographical map, and this is sometimes visible with the ordinary loupe.

The cortex of the lens increases with age as we would expect, knowing that the lens grows throughout life. The surface of the lens besides its suturing exhibits a peculiar shagreen; an example in ordinary life is seen at the surface of books bound in Morocco leather. This shagreen becomes modified and then disappears as a lens becomes progressively cataractous.

Certain congenital anomalies have been discovered in the lens and those already known have been examined and described in more detail. In connexion with remains of pupillary membrane fine filaments are sometimes adherent to the anterior surface of the lens, whilst in other cases the only remnant is a collection of fine brown stellate cells in the pupillary area. Almost constantly the remains of the hyaloid artery may be found down and in from the posterior pole of the lens, taking on the form of a small opaque disc to which is attached a short cork-screw like structure. Several cases of posterior lenticonus have been described although the condition does not appear to be strictly congenital as the fœtal nucleus in all cases has been found intact. The conical backward bulging causes a circular convex surface at the base of the cone to be presented forwards towards the light. Being a convex mirror it causes a circular reflex (the reflex of Vogt) which is also seen in connexion with the bulging backwards of Descemet's membrane in disciform keratitis. Posterior lenticonus is always associated with cataract in the posterior cortex. A common congenital opacity is seen in the form of tiny brilliant white dots at the level of the anterior Y of the fœtal nucleus. This suture may also show marked opacity, known heretofore as stellate cataract.

CATARACT.

Anterior capsular cataract is rare and is surrounded by a peculiar halo where no shagreen is seen. When anterior polar cataract is present its connexion with early life is shown by the fact that it may be reproduced at the surfaces of discontinuity in connexion with the fœtal and adult nuclei. Zonular cataract may occur as a congenital or an acquired condition and we may judge as to which it may be by its size and position. The opaque disc is seen to be formed of tiny white dots, a condition usual in all forms of nuclear cataract. Riders are commonly present, and Vogt has pointed out that they are often in the immediate neighbourhood of clear gaps in the periphery of the opacity.

Among the senile changes which occur in the lens the slit-lamp has been able to demonstrate that many changes, non-cataractous in nature, are commonly seen. These changes may or may not be associated with senile cataract.

As compared with that of the child the lens of the old person shows an increased internal dispersion of light. This is often associated with a deepening of the colour in the posterior part of the lens which is yellowish in appearance. This is partly due to the normal fluorescence of the lens whereby the light passing to the posterior part of the lens is deprived of some of the blue rays, and, after reflexion from the back of the lens, is further filtered before it reaches the observer; the result is that the rays from the red end of the spectrum predominate. Crystals with red or green reflex are sometimes seen. An almost constant feature is the formation of a relief at the surface of the adult nucleus and this may be examined best in the zone of specular reflexion. When performing an examination by retinoscopy one often finds a good deal of irregular refraction in the lenses of older patients. This is now demonstrated to be

* Parts I. and II. appeared in our issues of August 16th and 23rd respectively.

due to the formation of clefts filled with clear fluid occurring in the more superficial parts of the lens. They may arise in the site of a suture, when they are often regular in outline and may occur elsewhere among the fibres of the lens, where they are very irregular in outline. They make their appearance after 50 years of age, and are usually associated with lens opacities.

The slit-lamp has allowed us to observe a new phenomenon in the senile lens, which is usually associated with cataract. It is known as *lamellar separation* and is situated in the middle and deep layers of the cortex. It consists of a series of parallel lines running up and out from the lower nasal part of the lens. It is much more frequently seen in the anterior than in the posterior cortex.

From the clinical point of view the slit-lamp is so useful that it is possible to arrange the various types of presenile and senile cataract depending largely upon the layers of the lens in which the opacity occurs.

A very common type of presenile cataract seen in 25 per cent. of adults is *coronary cataract*. It interferes little, if at all, with vision since it is situated in the periphery of the lens and is only uncovered if the pupil be fully dilated. The opacities are thin so that they may be missed with the ophthalmoscope. They are club-shaped, nummular, or annular and appear blue or brown, depending upon the incidence of light. Another type of presenile opacity is *dilacerated cataract*. It is moss-like in appearance and appears, possibly congenitally, in the deepest part of the adult nucleus. *Cuneiform cataract* has been usually described in the past as peripheral striæ. These opacities occupy the deepest cortex, are whitish in colour, wedge-shaped, and occur both in front and behind the adult nucleus meeting by their base at the periphery of the lens. Dust-like cataract in concentric layers appears as very small opaque dots in the surface of the adult nucleus and the adjacent cortex. Posterior saucer-shaped cataract is usually described as posterior cortical opacities. It occurs in the most posterior layers of the cortex as a single layer. The opacities are dense and may be vacuolated and crystalline. Although it may not be very apparent with the ophthalmoscope, nevertheless it affects vision considerably and calls for early operation. Fortunately, the lens is considerably sclerosed so that extraction is not unduly difficult.

The opacities so far described which occur in the cortex are usually fairly gross in size contrasting with nuclear opacities which are usually minute.

Nuclear changes are seen in three forms: central hyper-refringence, black cataract, nuclear cataract proper. At the time when practically all we knew of the surfaces of the lens was their property of acting as mirrors producing images of Purkinjé, in certain cases it was noticed that two small subsidiary images appeared between those produced by the anterior and posterior surfaces of the lens. These were found to be produced by the anterior and posterior surface of the nucleus, and when it occurred it was noticed that the eye suffered from a marked degree of negative abberation. The condition was called false lenticonus. The slit-lamp has shown that there is an increase in the optical density of the nucleus of the lens. This increase begins in the anterior part of the fœtal nucleus, then the rest of the nucleus becomes involved and the central interval is filled up. The result is that the nucleus becomes homogeneous and of increased density throughout. In *black cataract* the increase in optical density of the fœtal nucleus is accompanied by a yellowish coloration especially well marked in the posterior part. This coloration may be red-brown or black. These changes in the nucleus are usually accompanied by senile changes in the cortex. In *nuclear cataract* proper there is a diffuse increase in optical density of the nucleus associated with actual opacity which begins in the deep layers of the fœtal nucleus, finally enveloping the adult nucleus. Here again there are usually senile changes generally of a cataractous nature in the cortex. *Injury* may cause dislocation of the lens, and when this takes place into the anterior chamber the slit-lamp allows a more detailed examination than is otherwise possible. Subluxation of the lens is practically always associated with prolapse of vitreous into the anterior chamber; in such a hernia of vitreous of greater or less size may be seen protruding through the pupil and covered in tiny brown particles of uveal pigment.

Peculiar changes are seen in the anterior capsule of the lens in glass-blowers and others who work with a furnace. The change consists in a peeling off of the most anterior layer of the capsule, known as the zonular lamella. The anatomical features of Vossius' ring, produced in the lens by a blow upon the eye, have been explained. The condition is now known as traumatic annular deposit. The ring consists of a circular deposit of brown amorphous granules on the capsule of the lens, actually an impression of the pupillary margin. Traumatic cataract appears in different forms depending upon whether the lens capsule has been opened or not. When the capsule is intact a characteristic opacity appears as a white rosette in the posterior cortex just under the cortex. This cataract is easily distinguished from other types of posterior conical opacity by its rosette shape and the fact that there is no lustre upon its surface. The prognosis of this condition is good. Occasionally a portion of the opacity persists, and if this occur in a young subject it may become buried in newly formed lens fibres, the result being a traumatic lamellar cataract. The slit-lamp allows us to judge the date at which the accident occarred by the relative depth of the lesion, the deeper the opacity the older the lesion. When traumatic cataract follows a perforation of the capsule a localised opacification and swelling of the lens fibres results. This is usually progressive and is associated with a rosette at the posterior cortex. The earliest signs of siderosis are seen in the lens, a group of tiny brown dots appear first beneath the capsule just outside the pupillary opening consisting of iron impregnating the epithelial cells of the capsule itself. Later the lens becomes of a uniform brownish colour and the various zones of discontinuity disappear. When a particle of copper or an alloy of copper remains in the eye a greyish-blue cataract which is very thin is found, and the anterior and posterior surfaces of the lens take on a brilliant polychromatic lustre as if the lens had been plated with copper

Besides the changes in the anterior capsule mentioned previously other changes are produced in the lens in furnace workers. The disc line opacity at the posterior hole of the lens is well known. Some light has been thrown on the origin of this type of cataract by experimental work with infra-red rays focused upon the lens. In less than an hour cortical opacities may be produced. Recently considerable attention has been paid to certain changes that may take place in the superficial layer of the capsule in which a bluish lace-like membrane appears on the surface of the lens and peels off in small pieces. The importance of this process is that it is a cause of glaucoma (Glaucoma capsulo-cuticulare).

We are able to distinguish *complicated cataract* from other forms by certain marked appearances that have been demonstrated with the slit-lamp. The earliest change in the lens in the appearance of a polychromatic lustre at the posterior hole of the lens.

This appears before any opacity can be seen in the lens and consequently is of prognostic importance. The opacity that subsequently appears involves several layers of the posterior cortex and advances axially, in contrast with the posterior cortical opacity in senile cataract.

A whole series of cataracts of peculiar appearance has been demonstrated by the slit-lamp; these apparently arise in connexion with general diseases in which there is apparently some deficiency in the internal secretion of one of the glands. Roughly speaking these cases are similar in that the opacities are relatively small and appear in the superficial layers of the cortex just underneath the zone of disjunction. The diseases in which these opacities are found are myotonia atrophica, post-operative tetany, traumatic myxœdema, mongolism and cretinism.

Diabetes has been stated to be a frequent cause of cataract, but it is only recently that a type of cataract peculiar to diabetes has been described. In the early stages the appearance is quite characteristic; a great number of tiny opacities in the most superficial layers of the cortex gradually fading away into the substance of the lens and the appearance of small water clefts.

The Anterior Third of the Vitreous.

Only the anterior third of the vitreous can be examined by the slit-lamp, and unless the pupil be dilated only a very small portion in the axis of the eye. The normal vitreous differs in its visibility in different persons, but in a case in which it can be well seen the vitreous appears in a framework which is moderately luminous and an optically empty fluid portion. This appearance is maintained in such a way, that although the structure oscillates in movements of the globe, yet when the eye comes to rest the original pattern reappears. In old age a characteristic appearance of the vitreous is sometimes seen. The strands of the framework become broken and small white irregularities appear on them. We have already noted the constant scattering of tiny particles of uveal pigment in the vitreous in contusion of the eye, and when the vitreous is prolapsed into the anterior chamber in dislocation of the lens or after discission of the posterior capsule. When there has been a perforating injury of the globe with prolapse of vitreous the framework of the vitreous is dragged towards the perforation in a characteristic manner and is a permanent change. In inflammation of the uveal tract we may see a complete destruction of the vitreous framework together with the appearance of opacities which are deposited on the fibres or float apart in the more fluid parts. The appearance in vitreous hæmorrhage is surprising. Unless the hæmorrhage is very gross and there are large clots in the vitreous visible by ordinary methods of examination we see fine white opacities deposited on the fibres of the framework and small reddish opacities, apparently blood corpuscles. It has commonly been stated that synchisis scintillans is due to cholesterin crystals in the vitreous. The appearance by the slit-lamp does not support this suggestion, since the opacities have not the form of crystals but of glistening white globules strung together like beads.

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SPECIAL ARTICLES

BRITISH MEDICAL ASSOCIATION.

ON August 28th, during the annual meeting of the Association at Winnipeg, Sir WILLIAM WHEELER delivered a clinical address on the significance of

Recoil Following Visceral Decompression.

Excluding traumatic and acute inflammatory conditions, he said, a large number of the patients who sought advice suffered directly or indirectly from the effects of pressure or back pressure on an organ or system. An external stress acting slowly was followed by a mechanical adaptation; acting quickly, it might produce a strain sufficient to rupture or irreparably disturb an organ or system. Unrelieved, it led to secondary pathological phenomena and, if suddenly relieved, the recoil might cause cell rupture, vascular derangement, or disturbances to the nervous mechanism. The change produced in an organ by gradually-increasing back pressure was probably primarily vascular. The direct pressure, combined with reflex vasoconstriction, closed some of the capillaries, thereby causing decreased blood-supply and function. On sudden removal of pressure the capillaries expanded and, with the removal of the vasoconstrictor reflex, the arterioles also dilated, flooding the organ with blood. Cellular œdema, vascular stagnation, and functional collapse supervened. Treatment appeared to be governed by the universal principle that the greater the pressure the more gradual should be the relief. This principle applied to "medical," "anæsthetic," and "obstetric," as well as to "surgical" back pressure. Patients with back pressure in the heart were treated by those drugs which had the slowest and most prolonged action; if it were possible to reduce the blood pressure suddenly the cure would certainly be worse than the disease, for failure of heart and kidney would inevitably follow. Anæsthetists used spinal injection or chloroform cautiously if their patients had high blood pressure, for the rapid fall induced by these methods might produce an alarming reaction. The oculist dealt with glaucoma by gradual withdrawal of aqueous humour and avoided retinal detachment, vascular dilatation, and intra-ocular hæmorrhage by gradual decompression. If a hydramnios formed rapidly the circulation suffered and the patient complained of cyanosis of the lips, hands, and feet, and of indigestion and vomiting. If the membranes burst, however, the recoil caused syncope. The obstetrician laid special stress on making a very small or valvular opening in the membranes to ensure that the waters escaped slowly. Again, if the fluid from a hæmatocolpos were not drained slowly the patient might suffer extreme shock. In the realm of the obstetrician there was a striking example of accommodation to ever-increasing intra-abdominal pressure and to its release. M. Remy, however, had suggested that the evil results of release of pressure might be seen even in normal childbirth; death might occur without any lesion by a sort of

inhibition on the heart, as he put it, from the abdominal sympathetics.

THE KIDNEY AND LIVER.

Back pressure in the urinary tract was comparatively well understood. Cardiovascular disease kept company with prostatic enlargement in about 42 per cent. of cases, and improved as the renal function was restored. Gradual decompression was advisable in all cases, whether there was evidence of back pressure or not. Rapid emptying of a distended bladder by any means might be followed by acute œdema and congestion of the urinary tract, resulting in loss of function. These destructive changes contrasted vividly with the repair changes which followed decompression. A certain amount of regeneration of the epithelium of the tubules had been seen after incision or after the relief of hydronephrosis. The principal aim of decompression was to save any kidney tissue which had survived the destructive action of back pressure, for a very little renal tissue was enough for healthy life. The careful relief of decompression was accompanied by the disappearance of symptoms, but haphazard methods would not give uniformly satisfactory results. The van Zwalenburg method allowed the urine to trickle into a receptacle adjusted at the right level above the bed, and took two to eight days to empty the bladder. It was not safe to withdraw small amounts every few hours or to empty the bladder and partly refill it with some solution; both these methods produced sudden decompression.

Sudden relief of pressure on the liver was not so risky as sudden emptying of the bladder, since back pressure acted more slowly and less gravely on the cells of the liver. Nevertheless, sudden decompression sometimes caused cessation of hepatic function. Hepatic shock and insufficiency were not properly understood, but it was known that liver cells possessed a high degree of recuperative power and that measures for gradual vascular decompression—e.g., the Talma Morison operation—stimulated this recovery. Slow drainage of the gall-bladder or common duct in cases of biliary obstruction permitted this regeneration. Pressure causing loss of function was revealed by the appearance of white bile. When sudden operative decompression caused liver shock there was sometimes a free flow of bile, followed later by cessation and symptoms resembling those of uræmia.

ASCITES AND INTESTINAL OBSTRUCTION.

Even modern methods of withdrawing fluid from the abdomen were sometimes followed by cachexia, syncope, or hæmorrhage into the intestines and abdominal walls. Jaundice and grave nervous symptoms had been known to follow paracentesis in cases of cirrhosis. Since it was impossible to foresee these serious symptoms, the only safe course was to provide for very gradual decompression.

The gradual reduction of pressure in the distended large intestine, induced by preliminary drainage, probably accomplished far more than mere relief of toxæmia and restoration of the tone of the bowel and the size of its lumen. The intestine might show more repair after decompression than we yet knew of. In acute cases there was still a high mortality, and many suggestions had been put forward to account for this. Sir William Wheeler felt that, in his experience, acute cases did best when a slow, steady drain could be established through a small tube. Rapid drainage through a Paul's tube might be followed by deplorable results with the clinical picture of general shock. The results were always good if the obstruction could be relieved simply—by dividing a band, for instance—and the intestinal contents evacuated naturally, but a small enterostomy tube acting as a safety valve gave equally good results and was essential in all but the earliest cases.

EMPYEMA.

Any change of pressure on one side of the mediastinum was accompanied by an almost equal change on the other side. Aspiration and slow decompression of empyemata had reduced mortality from 40 or 60 per cent. to 5 or 10 per cent. When intrathoracic pressure was high the intercostal spaces bulged and the mediastinum, liver, and diaphragm were displaced. If the pressure were suddenly released the result might be an acute pulmonary œdema or a to-and-fro flapping of the mediastinum which affected blood æration and circulation, producing a condition of shock which often caused death. The line of safety was to aspirate or drain with a catheter before evacuating, whether the pressure was high or only moderately raised, or whether the infection was streptococcal and diffuse, or pneumococcal and associated with adhesions. Occasionally simple aspiration was followed by fatal collapse. This was probably not due to vagal reflex as had been suggested, but to flapping mediastinum.

CEREBRO-SPINAL DISORDERS.

Lumbar puncture might do harm or even kill the patient when performed during high intracranial tension. This was often due to wedging of the bulb in the foramen magnum, with resulting anæmia and paralysis of the vital centres. Lumbar puncture was especially dangerous in cases of hydrocephaly due to tumour, and often caused giddiness, headache, nausea, vomiting, and rigidity of the neck muscles. Ill-effects were, however, very seldom produced if a small-bore needle were used and the fluid withdrawn very gradually, the decrease of pressure being controlled by a manometer. Spinal compression might be aggravated by lumbar puncture and the signs and symptoms become worse; this effect might be of diagnostic advantage. In some cases the root pain became more severe and in others moderate motor and sensory disturbances were followed by complete paralysis. Analogous changes might be seen in cases of intracranial growth. This diagnostic aid, however, demanded a price which might be severe unless the amount of fluid and the rate of withdrawal were carefully controlled. Lumbar puncture was of decided value in the treatment of acute anterior poliomyelitis and posterior basic meningitis, but a sharp distinction, Sir William Wheeler concluded, must be drawn between diagnostic puncture, which was safe, and medical decompression, which might be dangerous.

THE CANCER HOSPITAL, FULHAM.—Last year there were 1162 new in-patients and 1557 new out-patients, a substantial increase in each class. These larger numbers are to some extent accounted for by the work done with radium, cases being received for much shorter periods, and many more operations being performed, and to the gradual education of the public in the importance of seeking expert advice in the early stages of disease. Although the hospital at present remains entirely free, "some means of encouraging, if not actually inviting, patients to contribute as far as possible may," the report says, "before long be devised." The hospital has been using radium since 1903. The new buildings for the electrical and radiotherapeutic department will cost £93,000, without counting equipment, instruments, appliances, &c. The appeal to the public has so far produced £17,500.

MEDICINE AND THE LAW.

Miners' Nystagmus and Compensation.

ANY general system of insurance against, or compensation for, accident and ill-health demands good faith. In particular the provisions of the Workmen's Compensation Act which treat certain industrial diseases as accidents of the employment must protect the employer against liability where all-important information has been suppressed or false information deliberately given. Thus Section 43 of the Act declares that compensation shall not be payable "if it is proved that the workman has at the time of entering the employment wilfully and falsely represented himself in writing as not having previously suffered from the disease." The principle is simple enough but occasionally there is doubt whether the date of the false representation synchronised with the date of entering the employment. Where work is intermittent, difficulty arises; the House of Lords had a difficult case of this nature to examine lately. The disease was miners' nystagmus. The first relevant fact in the workman's history was that in 1895, when disabled by the disease, he finally settled his claim against his then employers for a lump sum payment. His subsequent work was done for a different firm of coalmasters by whom he was employed at the following intervals. He first worked for them in March, 1926, then went to Canada, but came back to them in April, 1927. Up to this point he had made no declaration. A few days later, however, he went to another section of the colliery where, in his work as a miner and brusher, he came under a different brushing contractor. He then made a written declaration (found to have been wilfully and falsely made) that he had at no time suffered from miners' nystagmus. Trade became slack and he was paid off in July and thereupon received unemployment insurance benefit; he came back in August (under the same contractor) and was paid off again in September. On Nov. 7th (1927) he came back once more and again made the false declaration. He remained at work till April, 1928; he made the declaration a third time when he worked one shift on a date in May. Otherwise he remained in receipt of benefit till June 15th, from which date he worked till August 26th. A few days later he was certified as disabled by miners' nystagmus as from August 26th; he has since remained totally incapacitated from that cause. The Scottish tribunal of first instance awarded him compensation, the arbitrator considering the man to have been continuously employed from April 27th, 1927, down to August 26th, 1928, except for the periods when unemployment was temporarily due to bad trade. As no declaration had been made on April 27th, the arbitrator saw no obstacle to the award of compensation. Was this decision as to the continuity of employment from April, 1927, onwards a decision of fact which could not be disturbed on appeal? The Court of Session felt itself able to re-open the matter and the House of Lords has confirmed that Court's view. Under the Act the industrial disease may be referred to any employment during the previous 12 months; compensation is recoverable from the latest employer, but the latest employer may join up a former employer in whose period of employment the disease is proved to have been contracted; if the disease is of a gradual character, each of the successive employers must bear his share of liability in the proportion determined by the arbitrator. In this sense employment for the previous 12 months is looked upon as one employment. This being so, the House of Lords decided that the employment which extended during the final 12 months before the certificate of disablement was the employment which began on Nov. 7th, 1927. The workman's entry into employment on that day synchronised with one of his false declarations; consequently, no compensation was payable.

The merely ethical view of the case (under which it would make little difference whether the false representation was made in November or a month earlier or later) is immaterial. The popular view may welcome adequate compensation and proper medical treatment for a miner suffering from nystagmus, but may grudge him the power to capitalise his total incapacity at frequent intervals at the expense of successive employers. Medical opinion may regret that significant information of the previous history of a specific industrial disease should be so easily hidden. If the recent case under discussion is not to be repeated, frequent medical examination of workmen and an elaborate system of filing their personal records might be of assistance. But employers deprecate the regimentation of industry, and workmen would have a right to resent the calendaring of personal details suggestive of the finger-print system of Scotland Yard.

Dangerous Drugs.

Geoffrey Bradford Wilmer, otherwise Melville, pleaded guilty at Maidenhead police-court on August 27th to six summonses under the Dangerous Drugs Consolidated Regulations charging him with unlawful possession of 300 tablets containing diamorphine chloride. He had been arrested at Northampton on a warrant issued last December, when a medical practitioner was convicted of offences under the Dangerous Drugs Acts. Wilmer, it was stated, had obtained the heroin from a duly qualified chemist in Maidenhead on the faith of prescriptions signed by Starkie, a London doctor whose name was removed from the Medical Register in 1922, a fact of which Wilmer was well aware. Wilmer made a long statement to the bench; subsequently Chief Inspector Prothero gave the court such information as the police had ascertained. Wilmer, he said, had represented himself as Major Wilmer and as Major Melville; he had also been known as Captain Nicholls and, at Melton Mowbray, as Captain Carter. Wilmer denied having used these names; he produced a bill for 170 guineas for medical treatment on which he was apparently described as Captain Arnold. The police-inspector stated that Wilmer claimed to have been an officer in the Essex Regiment, retired with the honorary rank of captain, and to have received shrapnel injuries in the war. He had not, in fact, been wounded in the war; he held no honorary rank as an officer, but was an imposter. The magistrates sentenced Wilmer to six months' imprisonment.

When the strict regulation of the possession and supply of drugs is taken into account it may seem surprising that it was possible for a man like the accused to be in possession of a considerable supply. In another case, disposed of at Wolverhampton some days ago, a medical practitioner who had become a drug addict was stated to have been supplied during a period of 11 months with 484½ gr. of cocaine, 825½ gr. of morphine, and 1912 drachms of liquid morphine. A doctor, by virtue of the general authorisation under the statute and statutory regulations, can, if he cares to abuse his authority, obtain supplies from different chemists by representing that the drugs are required for dispensing purposes. But a layman

like Wilmer has no such opportunity. The explanation in Wilmer's case is twofold. From statements made by Wilmer to the police, it appears that Dr. Starkie furnished him with a number of signed sheets of notepaper in blank; when Wilmer wanted a drug he filled up the sheet, which thus became a prescription. Wilmer also stated that, by an understanding with Dr. Starkie, he took whatever heroin he required out of drugs obtained on prescriptions in the name of a Mrs. Melville. A chemist, to whom the prescriptions were presented, was unaware that Dr. Starkie was an unregistered practitioner; he took the very proper precaution of communicating with him by letter and by telephone, but was reassured by the answers he received. The second explanation of Wilmer's success in obtaining supplies was that a chemist, again very properly, traced Dr. Starkie's name in the Medical Register, but in a copy for the year 1921 (before the name had been removed). Where chemists have taken such precautions it is certain that no magistrate or judge would encourage the taking of proceedings against them under the Dangerous Drugs Acts and Regulations; the police, therefore, are unlikely to initiate such proceedings. But the incident suggests the question whether it is part of a chemist's duty to possess an up-to-date copy of the Medical Register. It also suggests the further question whether the police, who apparently had had Wilmer's movements and purchases under observation for some time, do all that they can to warn chemists in any neighbourhood where a known drug addict is suspected of breaking the law. Though the facts in Wilmer's case do not justify the suggestion, there is sometimes a popular impression that the police are more anxious to accumulate evidence for a substantial conviction than to prevent the commission of crime. This impression will not be removed by the allegations in another case a few days ago where a man, described as a laundry canvasser, pleaded guilty to unauthorised possession of 56 g. of cocaine. The detective-inspector on that occasion had admittedly posed as a dentist; he had apparently said he was a sleeping partner in a firm of dentists, had produced £32 in notes, and announced that he could do with half a pound of the drug. Mr. Cairns, in passing sentence of three months' imprisonment, remarked that he would have imposed the maximum of 12 months if the circumstances had been different. Though full allowance must be made for the difficulties of suppressing the drug traffic, the magistrate may have shared the popular distaste for a situation created by a member of an English police-force turning himself into an *agent provocateur*. The restrictions on the supply and possession of dangerous drugs will not easily be enforced without the willing coöperation of medical practitioners or dental and veterinary surgeons. That coöperation will be more smoothly secured if their respective professions are not peopled with imaginary rascals created by the romantic inventiveness of the guardians of law and order.

HOSPITAL FOR SICK CHILDREN, GREAT ORMOND-STREET.—In 1929 this hospital admitted a record number of in-patients—7247—whose average cost was £6 5*s*. 10*d*., and there were 29,348 new out-patients. At £67,200 the income increased by £13,153, most of which was accounted for by larger legacies and an increase of over £3000 in receipts from the Hospital Saving Association. The expenditure was £60,319. The special clinics for rheumatism and asthma have proved most valuable; a new department devoted to guidance in matters of child welfare has also been started. Increasing demands upon the hospital have satisfied the board of management that the project of reconstruction cannot longer be delayed.

PARIS.

(FROM OUR OWN CORRESPONDENT.)

OVERCROWDING OF THE MEDICAL PROFESSION IN FRANCE.

YOU have already noticed[1] the warning given so frankly and wittily by Prof. Carrière, of Lille. A report recently presented by Dr. Léon Bizard and Dr. Xavier Colaneri to the *Fédération des Groupements Médicaux* of the Paris area shows how startlingly rapid have been the changes which have produced a crisis in the medical profession in France, owing to the great increase in the numbers of medical students and doctors. In 28 years the number of doctors has increased by 10,685, whereas the total population of the country has increased by only two millions in the same period. In the four-year period 1925–28 there has been an increase of 3350 doctors, Paris and its suburbs alone having been presented with more than a thousand new medical practitioners. Two main factors are held responsible for this abundant invasion of the medical profession by new recruits. The first is the great attraction which the profession of medicine now has for women: in 1929 as many as 2730 women registered as medical students, the corresponding number of male students being 10,650. The other factor is the great number of foreigners who join the medical profession in France. Yet another factor is playing an important part, though its influence is difficult to assess in figures. It is the army of ancillary practitioners; nurses male and nurses female, masseurs and masseuses, soi-disant auxiliaries who yesterday were the assistants of medical practitioners, and to-day are often their competitors.

Dr. Bizard and Dr. Colaneri propose several remedies for a state of affairs which they consider deplorable. They recommend the addressing by a competent authority of a circular to parents, scholars, and teachers, stating the material and other obstacles at present obstructing the medical curriculum and profession. Doctors with university contracts would do well to give addresses on this subject in the schools of the country. An educational campaign would also be useful in guiding medical students into by-paths of the medical profession which are apt to be neglected, although profitable. Dentistry for doctors and the colonial medical profession are two such by-paths, the following of which would do something to relieve the present congestion in the large towns in France. A measure which would be rapidly effective in reducing the number of entrants to the medical profession would be to put up a barrage at the examinations. It is pointed out that in the Faculty of Law more than 30 per cent. of the examinees fail to satisfy their examiners, and the common tendency for these 30 per cent. odd to find consolation for their rejection in sweeping wholesale into the medical profession should be discouraged by raising the standard of the medical examinations. If all medical students had to submit to a written anonymous examination, and were obliged to abandon their medical studies after failing to pass their medical examinations on two or three occasions, the double purpose would be served of lessening the congestion and competition among doctors and of saving the public from an inferior class of practitioner. It is also hinted that candidates for a degree in medicine should undergo a medical examination, so that the

[1] THE LANCET, 1930, i., 1438.

would-be practitioner too deaf to auscultate a patient could be eliminated. It will be seen from the above remarks that the dangers of a medical proletariat and other bogies in the medical profession in France are to a great extent those which face it in many other parts of the world.

THE PASSING OF THE OFFICIAL BROTHEL.

While one civilised nation after another has abandoned the official regulation of prostitution, finding its so-called advantages a snare and a delusion, France is still officially pledged to this system. It may not be so for long. Indeed, there are already signs of a revolt against it, in the provinces at any rate. At Grenoble, for example, the municipal authorities have just decided to abolish the regulation of prostitution, and to shut the *maisons de tolérance* as from Jan. 1st next. Behind this official decision is the work of one man, Dr. Hermite, hospital surgeon and social worker, whose recent report to the municipal authorities showed in no uncertain terms what can be done by a system of free consultations carefully organised. During 1926 and 1927, and before his system of free out-patient consultations was started, the antivenereal service registered 691 male and 481 female consultations. During 1928 and 1929, after free out-patient consultations were started, the number of male consultations rose to 8449, and the number of female consultations to 4369.

HEALTH INSURANCE AND THE MEDICAL PROFESSION.

The medical profession in France has followed with not a little anxiety the development of social insurance in general, and that of the law of April 30th, 1930, in particular. The French medical profession is, in fact, only now beginning to face that problem which was more or less solved in England before the war, and at a still earlier date in Germany. Late in July the Confederation of the Medical Syndicates held a meeting in Paris to discuss the attitude of the medical profession to the new law. Dr. Dibos, who has succeeded Prof. Balthazard as President of the Confederation, was in the chair. Much dissatisfaction was expressed by various speakers at the conditions under which the medical profession would be obliged to work under the new law. It was, however, finally agreed by a vote of 13,001 to 1668 to collaborate *à titre d'essai* with the Government and all concerned in carrying out the provisions of the new law. Thus, while pledging itself to act in a civic spirit as far as possible, the medical profession reserves to itself the right to reconsider the whole question should necessity arise.

A WIRELESS CAMPAIGN AGAINST VENEREAL DISEASE.

How times have changed since the use of the word syphilis was forbidden in French telegrams! That enterprising broacasting station, Radio-Paris, has recently appointed a Social Hygiene Committee, presided over by Prof. Roger, and including such well-known names as those of Profs. Balthazard, Léon Bernard, Jean-Louis Faure, Gougerot, Marcel Labbé, Roussy, Tanon, Weill-Hallé, Chailley-Bert, Gautier and others. Prof. Gougerot opened a series of lectures on venereal disease, the titles of his remarks being: "What is Syphilis?" and "The Dangers of Undetected Syphilis." The reaction of the French public to this daring innovation was awaited with considerable interest. Three letters of expostulation were addressed to Radio-Paris on this subject. But as hundreds of letters of approval were simultaneously received, it is safe to assume that this educational scheme will be followed in its entirety.

THE BREEDING OF RAT-CATCHING CATS.

It is a curious fact that while for generations we have bred horses for speed and hens for laying, no one has systematically attempted to bring out and intensify by selective breeding the rat-catching qualities of cats. It is an extraordinary omission when one comes to think of it. A cat in whom the sight of a rat arouses no fiercer emotion than a mild and philosophical curiosity is almost unthinkable. Yet such has been the misconceived breeding of cats to fit them rather for the requirements of companionless elderly spinsters than for the destruction of rats, that a rat-indifferent or even a rat-fearing cat is now no uncommon sight. In view of these considerations it is reassuring to learn that the *Club pour les Chats Ratiers* of Havre has undertaken to organise a cat farm, the principal object of which is to breed genuine rat-catching cats. Dr. Loir, Medical Officer of Health for Havre, has already for four years been breeding cats for this purpose, and the port authorities and other interested bodies are contributing to the expenses of this undertaking, the results of which will be awaited with much interest by all concerned in the extermination of rats.

IRELAND.

(FROM OUR OWN CORRESPONDENT.)

HEALTH PROGRESS IN DUBLIN.

FOR the past half dozen years or so the ordinary municipal government of Dublin has been in suspense, and its functions have been performed by three Commissioners, appointed by the Government, one of the three being a medical man. Recent legislation has, however, made drastic changes in the municipal government of the metropolitan area. The city of Dublin is now to be joined in a "greater Dublin" with the suburban townships of Rathmines and Pembroke, while the seaside townships are to be amalgamated into a coastal borough, with its centre at Dunlaoghaire (Kingstown). Elections for the councils of these two boroughs are to take place very soon and, consequent on the establishment of the council of the new Dublin, the rule of the City commissioners will cease. Their chairman, Mr. Seumas Murphy, has taken the occasion to give to the press a summary of the work accomplished by himself and his colleagues since they took office in 1924. As regards its effect on the public health there is a record of sound and enduring work. The water-supply of the city has been increased, and a greater pressure made available in order to safeguard the supply to the higher areas on the north side of the city. Not only have the road surfaces throughout the city been improved, but modern methods of street cleansing have been introduced. As regards housing, a large programme has been carried out by Dr. Dwyer, the medical commissioner. When the Commissioners took control the number of corporation houses was 2279, whereas the number at present is 5992. The annual rental has increased from some £43,000 to £160,000. Over 900 more houses are in course of construction, and schemes are on foot for an additional 777. The staff for dealing with the inspection of meat has been increased, and the inspection itself, both for home use and for export, is thorough. A new city laboratory has been constructed and thoroughly equipped. There has been a great development of infant welfare work, with a gratifying decrease in infant mortality. Children's clinics have been

established, as also antenatal clinics, dental clinics, and violet-ray clinics, and a diphtheria immunisation clinic. A system of medical inspection of school-children was established in 1928 and in two years some 25,000 children have been examined. The record is one of which the Commissioners have every reason to be proud. It has always been recognised that the rule by commissioners must be a temporary phase in the history of Dublin, but it has been a fortunate period for the citizens.

SWIFT'S ASYLUM.

Another step of progress has been made by the governors of St. Patrick's Hospital, commonly known as "Swift's Asylum," in the opening last week of a new wing by the Governor-General. The hospital was founded in 1745 under the will of Dean Swift, who left almost all his property for the purpose. As he put it in verse some five years earlier:—

> "He gave the little wealth he had
> To build a house for fools, or mad,
> And showed, by one satiric touch,
> No nation wanted it so much."

As a matter of fact it was the first hospital for the insane to be founded in Ireland, and it remained the only one for some 70 years. The institution has always kept abreast of the best knowledge of the treatment of the insane and, like most other institutions of the kind, it has undergone great development in the last 30 years, during which time it has been under the medical superintendence of Dr. R. R. Leeper. In recent years a country branch has been established in a beautiful country house near Lucan, some half dozen miles from Dublin. The Governor-General, in declaring the new wing open, expressed his confidence that the hospital would continue to preserve the eighteenth century traditions of charitable helpfulness and of sympathetic efficiency, and that the governors would always, as now, recognise professional efficiency by removing obstructions to the application of steadily advancing medical knowledge.

THE MENTALLY DEFICIENT IN IRELAND.

At a meeting of the Dublin Rotary Club last week Mr. John Cooke, who has been for many years honorary secretary of the Dublin Branch of the National Society for the Prevention of Cruelty to Children, gave an address on "Feeble-minded Children," in which he pleaded strongly for legislation on behalf of this class in Ireland. He pointed out that the investigations of the Royal Commission of 1906 had been followed by ameliorative Acts for Great Britain, which were not made to apply to Ireland, although the need was relatively greater in Ireland. In the Irish Free State there were but two institutions for the care of feeble-minded children. Throughout the country, hitherto, numbers had been consigned to the workhouses, where accommodation and treatment were of necessity inadequate, or to the asylums. There were no arrangements for the separate teaching of these children, and hence the necessary educational treatment they should receive formed no part in the training of the teachers.

PUBLIC HEALTH SERVICES

REPORTS OF MEDICAL OFFICERS OF HEALTH.

THE following are 1929 statistics of six counties:—

Name of district and estimated (R.-G.) mid-year population.	Birth-rate.	Death-rates per 1000 of the population.					Death-rates per 1000 births.		
		All causes.	Tuberculosis.	Cancer.	Respiratory diseases with influenza.	Heart disease.	Infant mortality.	Young child (1–5 yr.) mortality.	Maternal mortality from childbirth.
Hampshire .. (432,600)	16·5	12·7	0·77	1·43	2·2	2·7	56	28	3·7
Norfolk .. (322,990)	15·4	13·4	0·76	1·67	2·3	2·4	60	22	4·4
Leicestershire (295,300)	17·0	12·3	0·99	1·37	2·4	2·0	57	35	4·8
Northampton-shire .. (216,500)	14·3	12·2	0·83	1·50	1·8	2·3	55	19	4·8
Cumberland (208,720)	17·7	13·3	0·88	1·48	2·6	2·4	74	34	3·8
Holland .. (89,400)	19·4	13·1	0·67	1·59	2·3	1·8	63	24	3·4

Stillbirths per 100 live births: Hampshire 3·7, Leicestershire 3·6, Northamptonshire 3·2, Cumberland 3·6.

Hampshire.

Dr. H. Leslie Cronk shows that most of the districts in the county are still served by medical officers of health who are engaged in private practice, so that the Local Government Act, 1929, with the consequent redistribution of county districts, will entail great changes by the appointment of whole-time medical officers of health and also by the abolition of the combined appointment of sanitary inspector and surveyor. The County Council will be able to take a hand in the provision of satisfactory water-supplies and drainage for small districts which at present lack such. It already does useful work under the Housing of Rural Workers Act.

Changes have been made in the scheme under which expectant mothers when booking midwives can insure against the need for medical help. In first pregnancies the premium is raised to 7*s*. 6*d*. and the insurance does not become effective until one month after the payment of the premium. The midwives attended 78 per cent. of the confinements. The percentage of calls for medical help was 42 for insured and 28 for uninsured cases. The net cost to the Council for each insured case was 7*s*., and for each uninsured 4*s*. 8*d*., and the total net cost was £1684. Experience in Winchester has shown that the maternity beds needed for emergency and abnormal cases are approximately equal, and the beds needed for these two groups are estimated at 44. The 40 abnormal cases admitted into the Hampshire County Hospital, Winchester, were: 22 of disproportion, 5 of toxæmia, 3 of antepartum hæmorrhage, and 10 others. All the mothers did well, but 4 of the children were stillborn. The 47 emergency cases admitted to the same hospital were 19 of toxæmia, 13 of obstructed labour, 10 of antepartum hæmorrhage, and 5 others. One mother died and the remainder did well. Of the toxæmia births, 8 were stillborn (2 macerated); of the obstructed labours, 7 were stillborn, and of the antepartum hæmorrhage, 5 were stillborn. The septic cases admitted under the Council's scheme numbered 29, of which 23 were received into the special isolation block of the County Hospital, and 6 to three other hospitals. New arrangements are in progress with regard to the fourth group of cases—namely, normal cases, where the home conditions are unsatisfactory. The services of an approved consultant were asked for in ten cases of

puerperal pyrexia and fever, six of whom were admitted to hospital. An investigation of the after-histories of cases of ophthalmia neonatorum, notified during the last two years, shows that in 1928 one child was blinded in one eye and one in both eyes, and that in 1929 one child was blinded in one eye and two children in both eyes.

Dr. Cronk is doubtful as to whether a campaign for immunisation of children against diphtheria should be pushed, but he thinks that general practitioners should be in a position to offer immunisation to those who desire it. A summary is given of the isolation hospitals provided by the 17 urban and 22 rural districts, and a scheme has been prepared for the elimination of unsatisfactory small hospitals and the concentration of beds in as few centres as possible.

There are in the county 2800 producers of milk. There is no routine veterinary inspection of the dairy herds, and the taking of milk samples for the discovery of tuberculous udders has not passed the experimental stage.

Norfolk.

Dr. T. Ruddock West states that it is hoped during 1930 to establish a comprehensive maternity and child welfare scheme, including health visiting and midwifery services, throughout the county. The number of parishes without a midwife in 1929 was 116, as compared with 186 in 1928. The births in the county numbered 4967. Midwives attended about half—1221 in their capacity as midwives and 1285 as maternity nurses.

In July, 1929, the medical, dental, and nursing staff of the school medical service were transferred to the public health department, and as the clerical staff was transferred in the previous year, the unification of the public health service is now complete. The public health committee has approved a scheme for the provision of isolation hospitals. The County Council already owns a site of 14 acres at East Dereham, with drainage, water-supply, electric light, gas, and land for extensions available, and a hospital will be erected on this site, which will provide for all districts at present without accommodation. The provision to be made for small-pox is still under consideration.

Under the orthopædic scheme there are two inspection clinics—at Norwich and King's Lynn—conducted by the orthopædic surgeon, Mr. M. W. Balman. The doubling of the cases seen as compared with the previous year shows that ascertainment is improving. Treatment clinics would be difficult to establish in this thinly populated county, and the treatment is at present given in the home by the (whole-time) orthopædic nurse, Miss J. E. Kemp, under the instructions of the orthopædic surgeon. The County Council contributes towards the apparatus required. At the end of the year there were 126 pre-school-children on the register, including 69 cases of rickets and 28 of congenital deformities. The tuberculosis officers use the services of orthopædic nurse, and call in the orthopædic surgeon when required. Twenty-two tuberculous children were using surgical apparatus at the end of the year. About 100 school-children also attended the two orthopædic clinics during the year. Short-stay hospital cases are accommodated at the Jenny Lind Hospital, Norwich, and long-stay cases at the orthopædic hospitals at Pyrford and in London.

There is a pressing need for accommodation for advanced pulmonary and surgical tuberculosis, which it is hoped will be met by the sanatorium to be established on the Stanninghall Estate of the County Council.

Leicestershire.

Dr. J. A. Fairer reports that an epidemic of small-pox began in July in the Shepshed and Ibstock districts, spreading to the western side of the county and to areas in the vicinity of Leicester. Chicken-pox was prevalent at the same time and in the Shepshed district the first cases of small-pox which occurred were not recognised for some weeks. The notifications received numbered 230, and there were no deaths. The two county hospitals were opened for the reception of patients in July and August respectively, and also admitted 62 cases from the city of Leicester. Of the 268 cases admitted, 246 had never been vaccinated, and among the vaccinated remainder there were no cases under the age of 35. There are three permanent and four temporary hospitals provided by the County Council for infectious diseases. Some of these are inadequately equipped and will be replaced by a combined sanatorium and isolation hospital to be erected at Markfield, in which there will be 54 beds for infectious diseases. In January the services of the county oculist, Dr. Constance Walters, were made available for pre-school children, and spectacles were prescribed for 11.

There were 362 notifications of diphtheria with 34 deaths, a case-fatality of 10·6. The deaths ascribed to influenza were 81 in the urban areas with a population of 120,900, and 156 in the rural areas with a population of 174,400. There are now 42 maternity and child welfare centres under the auspices of the County Council, as compared with 18 ten years ago, but antenatal work is only just beginning. The births numbered 5013, and the two antenatal clinics were attended by 39 and 53 mothers respectively. There are three hospitals and five out-patient clinics available for orthopædic work, but the need is pointed out for more systematic organisation in order to obtain continuity and to avoid overlapping. Dr. H. J. Blakesley, who conducts the male V.D. clinic at Leicester Infirmary, reports a serious outbreak of virulent syphilis there being 82 cases in the primary stage as compared with an average of about 15 for the past three years. Most of the cases showed a virulent form of actively infective organisms in addition to the spirochæte.

The River Soar was in a very polluted condition during 1929, owing partly to the excessive drought.

Northamptonshire.

Dr. J. M. Mackintosh took over the duties on Jan. 1st, 1930, following on the resignation of Dr. L. Meredith Davies in November, while Dr. Lila S. Greig acted during the interim. The report shows that the notification of births is incomplete. Of the 3104 live births, 242 were unnotified and of the 98 stillbirths only 61 were notified. Of 128 infant deaths investigated by the health visitors 77 died in the first month and 43 of the 77 were said to be prematurely born. In addition to the 15 maternal deaths, which make up the rate of 4·8, 6 other deaths investigated (on behalf of the Ministry) were associated with childbirth, one being a death from pelvic peritonitis due to attempted abortion. There were 14 cases of puerperal fever and 30 of puerperal pyrexia. In some cases the illness appeared to be concurrent only with the puerperium, and in one case infection was possibly due to a douche of milk and water given by a handywoman. Hospitals in Kettering, Stamford, Rugby, and Northampton are available for these cases and the same hospitals with the addition of the Warwickshire County Maternity Home for confinement cases. The last-named cases, numbering 48 during 1929, are those with unsuitable home accommodation and those whose confinement is likely to be abnormal.

Orthopædic treatment is provided in the county by the Manfield Hospital with its several out-patient centres. There were 29 known cases of small-pox with no deaths and 227 cases of diphtheria with a case-fatality of 5·7 per cent. There is a decrease in the attendances at the tuberculosis dispensaries but a large increase in the number of patients visited at home in consultation by the tuberculosis officer. The situation as to the examination of contacts is unsatisfactory. Young children are brought up by their parents, but young adults from 15 years onwards cannot be induced to attend. A very high proportion of pulmonary cases are only notified when hopelessly ill, and the hospital accommodation for advanced cases is quite insufficient. The tuberculosis officer,

Dr. G. B. Lord, also asks for hospital beds to enable artificial pneumothorax to be carried out satisfactorily.

Cumberland.

Dr. F. H. Morison says the noteworthy feature of 1929 was the fact that for the first time a complete maternity and child welfare scheme was put before and accepted by the County Council and only awaited the sanction of the Ministry of Health. Cumberland relatively to population, has made more use of the Housing (Rural Workers) Act than most counties. Forty-three applications have been received since last year and grants were sanctioned in every case. One application was subsequently withdrawn. The total assistance promised since the inception of the Act has amounted to £6745, about half of which has been already paid in respect of 67 dwellings.

Mr. R. Simpson, F.R.C.V.S., makes his second annual report on the inspection of the dairy herds. An increase of the veterinary staff has been sanctioned as it has not been possible to get round all the herds on the register. No opportunity is lost to educate producers not only in the hygiene of cattle but in the production of clean milk. Six outside complaints of tuberculous milk were received and three notices as to tuberculous milk in the county. In the investigation of these nine cases, the offending cow was discovered at the first examination in six instances. In one case the cow involved was detected and slaughtered in the district of another local authority. In the eighth case the result was negative, probably owing to the sale of cows, and in the ninth case the sample was from a large milk depôt which derived supplies from other counties and a negative result was obtained in the three Cumberland farms involved. The County Council have also instituted routine bulk sampling of milk in order to test for cleanliness and the presence of tubercle. Two hundred such samples were taken of which one-third reached the rather low standard for cleanliness, and three samples (1·5 per cent.) were tuberculous. The cows discovered and slaughtered with tubercle of the udder numbered 19, those with tuberculous emaciation 58, and those with other definite signs 66. Two cowkeepers were fined £5 each for failing to notify tubercle of the udder in an advanced stage, and another owner was fined £10 for failing to report a cow with advanced generalised tuberculosis. Mr. Simpson is of opinion that all the duties in connexion with designated milk should be carried out by the local authority.

Dr. Morison again complains of the inadequate arrangements and equipment of the V.D. clinics held at the Cumberland Infirmary, Carlisle, and at the Whitehaven and West Cumberland Hospital.

Holland.

Dr. H. C. Jennings shows that influenza affected the statistics adversely. The death-rate was 1·9 more than in 1928, and the infant mortality-rate 17 higher. Boston Borough had an infant-rate of 103 and Boston Rural one of 84. Diphtheria was more prevalent and 158 out of the 206 cases occurred in Boston and neighbourhood with 11 deaths. One of the 13 survivors from ophthalmia neonatorum suffered impairment of vision. Orthopædic clinics are to be held in the county in order to save the long journeys of patients to outside hospitals. The tuberculosis-rate was lower than ever before, but the rate in Boston is double that for the rest of the county. The dispensary is successful in securing the attendance of contacts for examination, and there are 30 open-air shelters loaned out to patients. Inquiries were made as to four confinements attended by unqualified women, and the need for a midwifery service subsidised by the County Council in the sparsely populated districts is pointed out.

On the night of Nov. 12th to 13th huge quantities of dead and dying fish passed down the River Witham as the result of gross pollution from the sugar beet factory at Bardney. The proprietors of the factory were prosecuted and fined £50, and it is understood that the effluents are to be treated according to the most modern practice in order to prevent recurrence. In January, 1929, a regional water committee was formed, and as a result a scheme for the water-supply of the whole district at a cost of £320,000 has been prepared by Sir Alexander Binnie, Son, and Deacon. A report by the county M.O.H., dated Sept. 5th, 1929, shows the water-supply of Boston to be grossly polluted. At that date the beck supplying the storage reservoir had been dry since June and the reservoir had become a pond of stagnant water. The new supply is to be derived chiefly from the Bourne springs which are boreholes sunk into a bed of the lower oolite, known locally as Lincolnshire limestone. Additional pumping plant will be needed to increase the supply from these boreholes.

INFECTIOUS DISEASE

IN ENGLAND AND WALES DURING THE WEEK ENDED AUGUST 23RD, 1930.

Notifications.—The following cases of infectious disease were notified during the week:—Small-pox, 93 (last week 95); scarlet fever, 1471; diphtheria, 953; enteric fever, 67; pneumonia, 474; puerperal fever, 52; puerperal pyrexia, 97; cerebro-spinal fever, 13; acute poliomyelitis, 15; encephalitis lethargica, 6; dysentery, 4; ophthalmia neonatorum, 101. No case of cholera, plague, or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the London County Council on August 26th–27th was as follows:—Small-pox, 209 under treatment, 4 under observation (last week 183 and 3 respectively); scarlet fever, 1632; diphtheria, 1810; enteric fever, 32; measles, 157; whooping-cough, 84; puerperal fever, 17 (plus 7 babies); encephalitis lethargica, 119; "other diseases," 25. At St. Margaret's Hospital there were 13 babies (plus 9 mothers) with ophthalmia neonatorum.

Deaths.—In the aggregate of great towns, including London, there was no death from small-pox, 3 (0) from enteric fever, 5 (0) from measles, 2 (0) from scarlet fever, 11 (1) from whooping-cough, 28 (11) from diphtheria, 45 (13) from diarrhœa and enteritis under two years, and 19 (1) from influenza. The figures in parentheses are those for London itself.

The deaths from enteric fever outside London occurred at Birmingham, Nottingham, and Oldham. No great town reported more than 1 death from measles or whooping-cough. Liverpool reported 3 deaths from diphtheria. Diarrhœa was responsible for 9 deaths at Liverpool, 3 each at Birmingham and Manchester.

The number of stillbirths notified during the week was 292 (corresponding to a rate of 42 per 1000 births), including 49 in London.

ST GEORGE'S HOSPITAL.—The annual report of this hospital records that 5120 in-patients were treated last year. Their average stay was 22 days, and they cost £15 0*s.* 8*d.* each. The 39,432 new out-patients cost 7*s.* 1*d.* per head. There were 250 births and 4286 operations, and 733 discharged patients were sent to Atkinson Morley's Convalescent Hospital at Wimbledon. A very large increase is reported in the work of the electrotherapeutic department. The income was £85,492 and the expenditure £86,483. The cost of maintenance is now more than double that of 1913.

THE NEW BETHLEM HOSPITAL.—In his annual report Sir Lionel Faudel-Phillips, the treasurer of the Royal Hospitals of Bridewell and Bethlem, states that the completion of the transfer of patients and the opening of the new buildings at Monk's Orchard will be an accomplished fact in the course of next month. Last year there were 416 patients, a smaller number than usual, because of the decision to close the hospital at Lambeth to new admissions before the reopening at Monk's Orchard. The average weekly cost per patient on ordinary expenditure was £4 13*s.* 9*d.*, but of the total cost (£46,312) £15,073 was provided by payments for patients varying from 2 to 3 guineas a week; 20 per cent. of the patients are on the free list.

CORRESPONDENCE

SULFOSIN THERAPY IN GENERAL PARALYSIS OF THE INSANE.

To the Editor of THE LANCET.

SIR,—Patterson and Switzer [1] have reported on Sulfosin Therapy in General Paralysis of the Insane, and they think that they did not obtain such a marked pyrexia as was to be expected according to Schroeder's paper. To this I may say that it seems to take some experience to obtain a maximal temperature with this treatment. For it has happened over and over again that physicians have written to me in this respect when they were first taking up the sulfosin treatment, but later, when I have instructed them in details on this point, they have always been satisfied with the results they obtained. It is my experience that the most favourable and reliable sulfosin effect is obtained by deep intramuscular injection—i.e., *supraperiosteally* on the lateral surface of the femur—preferably after a brief heating over a small flame (alcohol burner), by which means the sulfosin is dissolved completely. In this way I have employed the sulfosin therapy in 14 cases of general paralysis, and in 100 per cent. of these cases I obtained a temperature of or above 39° C. (102·2° F.), and in 57 per cent. of the cases a temperature of or above 40° C. (104° F.), leaving out the first two injections in each series that were given as test injections for the adjustment of the dose.

In fact, the various authors who have worked with this therapy (Shilvock,[2] Harris,[3] Marcuse and Kallmann,[4] Stiefler,[4] Jacobson and Smith,[4] Insabato [4]) have been satisfied with the pyrexia obtained—nay, in 15 patients Armenise [5] did even obtain a temperature of or above 40° C. (104° F.) in 13 cases (87 per cent.).

The pyrexia obtained with the sulfosin treatment may, therefore, be said to be satisfactory, and it bears very well comparison with the pyrexia of the malaria therapy. In addition, some authors (Warstadt,[4] Pires [4]) have found that several cases which had proved refractory to the malaria therapy were responding to the sulphur treatment.

Besides, the pyretic effects of the malaria and the sulphur treatments may hardly be compared by a simple tabulation of the maximal temperatures obtained. For the pyrexias are not identical in the malaria and the sulphur treatments. The temperature curve in the sulphur therapy differs considerably from the temperature curve in malaria therapy; in the sulfosin therapy the rise of temperature is of shorter duration than the fall, which frequently runs a remittent course, giving an unusually wide curve that is characteristic of the sulfosin effect. Indeed, it has been shown that the improvement in the humoral reactions is more pronounced in the sulfosin therapy than in the malaria therapy.

As to the inconveniences in the sulfosin therapy, I shall willingly admit that the reaction after the sulphur injection—in particular when it is effective—is accompanied by some pain at the site of injection. As a rule this pain does not set in immediately after the injection, but most frequently some hours later, it may be not until the temperature begins to rise. Generally these pains subside fairly rapidly, but tenderness and pains may persist for some days. These symptoms are treated with hot compresses (or alcohol compress) or electrical thermos-pillow, later on with massage. There is a great deal of individual difference in the sensitiveness to these pains, which unfortunately appear to be unavoidable if a favourable therapeutic effect is to be obtained. I have met with these pains in the response to every one of all the sulphur preparations I have tried out, and I have attempted, but in vain, to eliminate them in various ways—for instance, by injecting cocaine together with the sulphur. I have arrived at the conclusion that these pains are to be accepted as indicating that the organism is responding to the treatment with the desired reaction. As a rule the patients put up with these pains placidly and look upon them as an unavoidable discomfort. For these pains are by no means unbearable. This is evident from the fact that I have treated children of all ages without having to discontinue the treatment on account of pains.

I am, Sir, yours faithfully,

KNUD SCHROEDER, M.D.,
Physician-in-Chief to the Odense Hospital,
Odense, August 29th, 1930. Denmark.

[1] Patterson, W. G., and Switzer, S. R. L., THE LANCET, August 16th, p. 348.
[2] Shilvock, W. H., THE LANCET, August 16th, p. 347.
[3] Harris, N. G., Ibid., 1930, i., 1068.
[4] References, see Schroeder, K., ibid., 1929, ii., 1084.
[5] Armenise, D., Riv. di pat. nerv. e ment., 1930, xxxv., 326.

FATAL SYNCOPE FOLLOWING PERCAIN ANALGESIA.

To the Editor of THE LANCET.

SIR,—The following case of cardiac syncope during the induction stage of a percain intraspinal block should be recorded. A woman, aged 50, suffering from a very large multilocular ovarian cyst occupying the abdomen up to the costal margin, was given an injection of 14 c.cm. of 1 : 1500 percain in 0·5 per cent. saline, spec. grav. 1·003, between L1 and L2, and then placed in the prone position in order that the posterior roots should have a sufficient concentration of the drug. About three and a half minutes after being placed in this position she suddenly collapsed and died. She was turned on her back, the abdomen was opened, and the cyst punctured to relieve pressure on the diaphragm, and cardiac massage was performed with the usual restorative measures, but without success. The post-mortem examination revealed nothing remarkable in the heart.

This case shows without doubt that any attempt at the prone position in such cases is a tactical error. The weight of the trunk must very greatly increase abdominal pressure, and the contents may be thrust upwards against the diaphragm and pericardium. Furthermore, it is possible that the great vessels may be pressed between the spinal column and the tumour with great embarrassment to the circulation. It was the opinion of Dr. H. B. Weir, who conducted the autopsy, that the adverse mechanical conditions resulting in this case were the probable cause of the syncope. The amount of percain injected—between 0·009 and 0·01 g.—is so small that a general toxic effect can be excluded. One of the chief advantages of percain is that the amount required for spinal blocks is only a small fraction of the maximum dose permissible for infiltrations (0·2 g.).

The fall of blood pressure which occurs after spinal injections would be a contributory cause, especially in a case of this nature. For this type of case the prone position should, therefore, be abandoned, and

the patient may instead be kept for five minutes in each lateral position, with the head end of the table slightly lowered as a precaution. As percain injections are likely to prove useful in operative obstetrics, it is as well to remember that the gravid uterus presents a similar contra-indication to the prone position. With regard to normal administrations, the prone position has given rise to no difficulty, and a steadily increasing number of cases have been uniformly successful. No case has shown any involvement of cervical nerve roots.

I am, Sir, yours faithfully,

W. HOWARD JONES.

London, W., August 26th, 1930.

UNDESIGNATED PASTEURISED MILK.

To the Editor of THE LANCET.

SIR,—The annotation on milk-borne epidemics in your issue of August 16th (p. 359) mentions the pasteurisation of milk in Brighton. The one-third of Brighton's supply which I included as pasteurised is treated in every way as designated pasteurised milk would be. The pasteurisation is done not at the farm but by a few large distributors; thereafter the milk is bottled and capped before being handled, so that the risk of infection after pasteurisation is reduced to a minimum. This year infected milk from a farm was sent both to an urban area and to Brighton. An outbreak of scarlet fever resulted in the urban district, but not in Brighton; fortunately the Brighton supply was pasteurised by the retailer before distribution. This is a good practical example of the benefit of the process.

I quite agree with you that it would be better if all pasteurised milks were sold as designated milks, and when the public have realised the comparative safety of drinking pasteurised milk the retailers who pasteurise will sell their milk as designated milk. In the meantime the public, and indeed even doctors, are confused by the number of designated milks, and are not taught that the safest liquid milk from the point of view of tuberculosis and sore-throat infections is pasteurised milk.

I am, Sir, yours faithfully,

DUNCAN FORBES,
Medical Officer of Health, Brighton.

August 20th, 1930.

THE MEDICAL TREATMENT OF CANCER.

To the Editor of THE LANCET.

SIR,—We, in Liverpool, have long regretted Dr. Todd's somewhat—shall I say—irritating attitude in regard to our investigations, but we have endeavoured to treat him with every consideration, for we know—indeed he, himself, has stated this in print [1]—that he has felt that enough notice was not being taken of his publications. I am grateful to you, Sir, for tactfully correcting, in your leading article, the ridiculous insinuations which are contained in the following statement made by Dr. Todd: "This [Dr. Todd's] research *was commenced in 1925, shortly after the revival or rehabilitation* of the lead treatment of cancer was brought about at Liverpool. Lead is an old remedy for cancer; Ambroise Paré used it with success, and we (the plural used to include the team) have obtained some results from a modification of his method." (Italics mine.) Does Dr. Todd wish to imply that I have been guilty of plagiarism, and that he has followed Paré and not us? This would be a step forward in Dr. Todd's pretentions that his work is quite independent of ours. Admittedly, Dr. Todd *commenced his work three years after our first publication*, which was the result of many years' previous research. An interval of three years can hardly be described as "shortly after," to use Dr. Todd's words. Nevertheless, Dr. Todd in his first paper in 1927, and in his larger publication in 1928, acknowledged what we had done. It will be noted that his first paper appeared in the fifth year after our first communication to THE LANCET.[2] In this interval of five years we had published many other papers and addresses.

I had no knowledge, any more than Dr. Todd had, of the various, generally very curious, uses of lead in the treatment of "cancer" and other diseases made by early writers until Thomas's paper in French (1928) was brought to my notice, although I have referred to the knowledge of lead poisoning in ancient times. Indeed, if I had it would have interested me not at all scientifically, for doubtless every element has at one time or another been applied empirically, and some as panaceas for superficial lesions of all kinds. My reason for using lead was scientific and original, and will, I think, be so regarded by all fair-minded persons. Must we, I would ask Dr. Todd, regard the Good Samaritan and other benevolent persons of olden days, who used alcohol as a lotion for wounds, as the pioneers of antiseptic surgery? However, those interested will see some of this ancient history set forth on pages 388 et seq. of our book, "Some Aspects of the Cancer Problem." Perhaps this was the source of Dr. Todd's information. If so, he seems to have missed, or failed to profit from, the introductory paragraphs to that section, which are as follows:—

"The interest created by our work in the treatment of malignant disease with lead has led to a search through the literature, ancient and modern, to discover whether the remedy is a new one. The common fate, indeed, of all original work on a considerable scale is that it shall first be tested in respect of its value; then, if it be of proved worth, the literature from the time of the Ebers papyrus (circa 1500 B.C.) must be searched lest priority be claimed. This is right and proper, provided the historian has critical faculties." And the later sentence: "It does not appear that any indication was discovered of the special action of lead on malignant neoplasia until our own work was commenced in the year 1919; indeed, it may be stated with confidence that there is little in the literature to lead one to suppose that before the clinical work was started in Liverpool in 1920 any serious and scientific attempt had been made to treat malignant disease with lead."

I hope I shall never again be called upon to perform the distasteful task of meeting such a charge.

There are, too, certain matters of fact in Dr. Todd's paper and in your leading article on which I may be allowed, perhaps, to say a few words. From first to last we have advocated (the references can easily be found by anyone interested) the coincidental use of calcium and iodine. We have combined both of these in some of our preparations, and have always administered calcium lactate independently. A large supply of parathormone was sent to us from America soon after it had first been made, and we have used it in certain cases. So, too, with liver extract; for a long time we have employed this for the prevention and treatment of anæmia; and radiosterol we have used for infected cases. I do not know that we have especially referred to the last three in print, but they, and other adjuvants, have been employed not only by ourselves but by others when there have been indications. We believe that any practical physician would consider the exhibition of the last-named preparations as merely incidental.

The serious manner in which the writer of the leading article deplores the present state of the general medical treatment of cancer fills me with

concern. Even without lead so much can be done to relieve many patients, and I thought such methods were common in practice. The suggestions made to surgeons by Dr. Todd, which are summarised in the last paragraph of your leader, are all included in our paper which was published in THE LANCET in 1922.

It is interesting to learn, however, that Dr. Todd has discovered the error he made in denouncing the combination of lead and radiotherapy,[3] which we advised in our first paper. On the publication of Dr. Todd's first communication I wrote to him privately to call his attention to the fact that the "decidua" is not the "trophoblast," as he appeared to think. In my opinion, there is no excuse for a repetition of an error. Again, what does Dr. Todd mean when he writes in his present paper, page 391, column 2: "In addition, we found that the normal fat-splitting enzyme of the blood, which was usually increased in late cancer, showed a diminution when the treatment was being effective." When he made this statement on a previous occasion I again wrote privately to inform him that the augmentation of the pancreatic enzyme by the serum of cancer patients is reduced, as first shown by Shaw-Mackenzie, not increased—as Dr. Todd says—and that the administration of lead to these cases tends to restore this activity to the normal, and this is especially evident when they are doing well. My colleagues, Prof. Lewis and Dr. Corran, have published papers on this subject.[3 4] In our opinion, Dr. Todd's statements concerning this matter are the converse of the true state of affairs. Further, it is unfortunate that Dr. Todd should select a calcium compound to produce acidosis for the purpose of the prevention of lead storage. Acidosis certainly causes the liberation of ionic lead, but calcium actually leads to its storage, and we are in the habit of exhibiting calcium lactate for this purpose in order to avoid toxic manifestations, and have injected calcium chloride intravenously to mitigate these. Dr. Todd also tries to persuade his readers that we believe that the action of the lead is local only; I have frequently said that it acts constitutionally as well as locally, and this is based on experimental work, all of which has been published. Indeed, the researches of Prof. Lewis and Dr. Corran just mentioned indicate that beneficial changes are produced by lead in deranged body functions associated with cancer. We have, too, presented evidence that the action of lead is also local. This was evidently clear to the reviewer of our book, "Some Aspects of the Cancer Problem," in the *British Medical Journal*,[5] for he writes:—

> "The exact way in which lead deleteriously affects the cancer cell is not dogmatically stated, but it is thought to be probably both local and constitutional."

There is another point in regard to the general clinical aspects, both in Dr. Todd's paper and in your leading article which requires notice. Stress is rightly laid on relief in the disease as well as on cure. With regard to alleviation, I have time and again pointed out that this must be taken into account in any assessment of the value of lead therapy. On page 421 in our book mentioned above, the following sentence contained in a paper published in 1929 will be seen:—

> "Again, it cannot be too forcefully reiterated that in the early application of any new method, however important an absolutely curative effect may be, *arrest and alleviation of the disease must equally be taken into account. . . .*" (The italics are in the original.)

Nevertheless, clinical cures, such as we have obtained, are the ideal at which to aim, for obviously if they can be obtained alleviation will be more sure in the rest of the cases. Dr. Todd has apparently obtained no clinical cures of the disease.

As to lead selenide, to which Dr. Todd has almost exclusively devoted his attention, we have made this and other preparations of lead and selenium, and have found that the selenide has little value in comparison with other preparations. Lead selenide has not much, if any, abortifacient action; it has a low chemotherapeutical value, and, in our opinion, cannot be relied upon to affect malignant growth, hence the limited success of Dr. Todd. It is, in fact, not a preparation that should be employed to-day, for there are many better; indeed, this has been so from the commencement of our work. I hope soon we shall be able to say something about the more recent organic preparations made by Prof. Heilbron and Dr. Beilonsohn, which have given us good experimental results, and have, apparently, a satisfactory chemotherapeutical index.

For the sake of many patients who, if they knew the truth, would more readily submit to treatment, I must make it quite clear that in our hands it is very rare for any reaction at all to be produced by intravenous injections of lead preparations, and certainly injurious effects never occur at the present time. We have not seen a serious reaction for some years. There is a general impression abroad, and this is fostered by opponents of our methods and, I have reason to believe, by Dr. Todd himself, that severe reactions inevitably follow treatment administered by us. This is not so. Our preparations are as atoxic as lead selenide, and are very active, not comparatively inert as is lead selenide. Dr. Todd mentions, and in your leading article reference is made to, smaller dosage. In this connexion I would quote from a paper I published in 1928, as published in "Some Aspects of the Cancer Problem": "We have tended gradually to decrease the individual doses while aiming steadfastly at the administration of a high total quantity of lead—that is, 0·5 g. to 0·8 g. or a little more. . . . From this we may provisionally conclude that it is advisable to continue in a modified form the treatment over a longer period of time than previously considered necessary."

I am sorry to have to write this letter, but in view of all that has happened in connexion with our work it is necessary to insist that at least the truth be told, the literature be studied, and the work efficiently conducted, otherwise lead therapy in malignant disease will suffer at the hands not only of critics but also of friends.

I am, Sir, yours faithfully,

Liverpool, August 30th, 1930. W. BLAIR BELL.

1. Todd, A. T.: Brit. Med. Jour., 1929, i., 130.
2. Bell, W. Blair: THE LANCET, 1922, ii., 1005.
3. Corran, R. F., and Lewis, W. C. M.: Biochem. Jour., 1928, xxii., 451.
4. Lewis, W. C. M.: Rep. Internat. Conf. Cancer, Lond., 1928, p. 437.
5. Review, Brit. Med. Jour., 1930, ii., 63.
6. Bell, W. Blair: Brit. Med. Jour., 1929, i., 431.

RADIUM AND LEAD SELENIDE COMBINED.

To the Editor of THE LANCET.

SIR,—Dr. A. T. Todd has recently stated in your columns (August 23rd, p. 389) that radium treatment of cancer after lead selenide treatment not only has no retarding influence on the tumour growth, but causes tumours which had been held in check by lead selenide to spread rapidly and shorten life. He mentions 12 cases, but gives no details of how the

radium was applied. From this he argues that radium treatment has no direct action on the tumour cells, not even a retarding influence on their growth; and that the adverse influence of radium treatment is entirely a secondary effect. In view of the importance of this, perhaps we may ask exactly what X ray or radium treatment did these 12 patients have, and was the dose adequate? Recently at the Radium Institute there have been two patients who had several months' treatment with lead selenide, during which tumour growth ceased, but in which the tumours had not disappeared; they were given radium treatment (as under) with excellent results.

1. Male, aged 52, squamous epithelioma of neck. Lead treatment Sept. 20th, 1929, to March 20th, 1930. Tumour measured then 6·6 × 7·0 cm. On March 20th, 19 gold seeds 0·5 mm. gold, 1·8 mc. each, were inserted into the tumour, which rapidly disappeared, and on July 2nd patient was still free of disease and in good health.

2. Male, aged 54, secondary glands both sides of neck. Squamous epithelioma. Lead selenide Oct. 29th, 1929, to Dec. 18th. Aluminium seeds inserted into both sides on Jan. 1st, 1930, and 28th, when the tumours measured 5·5 and 6·0 cm. in diameter. On Feb. 17th the tumour on the right side measured 3·5 cm. and the left 5 cm. On July 2nd the right had disappeared, and the left was still growing. On July 14th the latter was again seeded.

It appears, therefore, that radium treatment after lead selenide treatment is not always followed by disastrous results.

We are, Sir, yours faithfully,

PHILIP GOSSE,
J. C. MOTTRAM.

The Radium Institute, 16, Riding House-street, W., August 30th, 1930.

TREATMENT OF PULMONARY TUBERCULOSIS IN SWITZERLAND AND AT HOME.

To the Editor of THE LANCET.

SIR,—I cannot agree with some of your correspondents that Dr. Harrison has overstated the facts. He has apparently a very intimate knowledge of the conditions of a winter cure in Switzerland, and although his statements may not apply to all patients or to all cure stations in the Alps, he has, speaking generally, drawn a very suggestive picture of the life of the average tuberculous patient wintering there. But there is one point which has not been stressed by any of your correspondents. I refer to the apparent declimatisation produced by a prolonged stay in Switzerland. Patients on their return home are more likely to relapse than those treated in our home sanatoria. They are more liable to catarrhal affections of the lungs and, as everybody knows, these affections are too often the forerunner of a process of reactivation in the old focus. If the patient finds that Switzerland suits him well, and if he is in a position to go out there winter after winter or, better still, if he is able to stay out there altogether, well and good. But if it is a question of six months there and back again to work in our "climate of perpetual damp and mist," then it is as well for him to undergo the treatment in a British sanatorium.

Dr. Amrein has not helped his case by his reference to "our perpetual damp and cloudy atmosphere." There are many localities from Land's End to John o' Groats where there is on the yearly average less mist and fog than in some of the best known "cure" stations in Switzerland. I have lived in the Upper Speyside district of Inverness-shire for the last 11 years, and I can say without fear of contradiction that I have seen less fog and mist in those 11 years than I saw for two winters spent in one of the most noted and best advertised Swiss resorts.

When the case is one where a very high altitude is indicated, and where the patient has to work for his living, I know of no more suitable climate than Southern Rhodesia. Entry is not difficult, provided the patient is sufficiently fit and is not likely to become a burden on the colony. For the last ten years I have sent many patients to Rhodesia after a preliminary cure here; most of them have made their homes out there, and the letters I receive from them are very encouraging.

I am, Sir, yours faithfully,

Kingussie, August 26th, 1930. FELIX SAVY, M.D.

TONSILLOMYCOSIS.

To the Editor of THE LANCET.

SIR,—In the early part of last winter I came across a fungus in a culture from the throat of a young woman. I did not recognise the condition until I read Castellani's article on tonsillomycosis in the January number of the *Practitioner*. Since then I have met with one other case, referred by Dr. Martin Edwards as a diphtheria suspect. This was a young man living on a croft. The tonsils, soft palate, and uvula were all patchy with creamy membrane, which peeled off leaving a slightly ulcerated surface. Direct smears showed monilia, and on blood-agar I got an almost pure culture. The chief symptom was unusual soreness on swallowing. Painting with solution of silver nitrate cleared it up in a day or two.

I am, Sir, yours faithfully,

JAMES CAMPBELL, M.B., Ch.B.

Lerwick, Shetland, August 16th, 1930.

INTRABRONCHIAL DRAINAGE.

To the Editor of THE LANCET.

SIR,—As is so rightly pointed out in your leading article of August 9th (p. 303), the mechanical factors in the course and treatment of such cases as bronchiectasis are of the greatest importance. One feels they require perhaps more attention than is given to them often, especially in the matter of mechanically assisting the patient to clear his chest. The bronchial blockage, the tenacity of the secretion, and the comparatively inefficient expulsive power from the bases of the lungs must all be taken into consideration. The poor emptying power of the lungs is usually helped by getting the patient to cough whilst leaning over the back of a chair, for instance, and this certainly helps, but it is not enough when one considers the bronchial obstruction and the thick tenacious fluid. Bronchoscopic methods are the only efficient and direct aids to the removal of the purulent material.

Of bronchoscopic instruments Chevalier Jackson's are the most satisfactory for this work on account of their lightness, good lumen, and practical adaptation to the needs that may arise. Those with proximal illumination, however, such as Haslinger's, have the advantage of throwing a powerful light well ahead of the distal end of the tube, so giving a good illumination of the area to be approached. Bronchial blockage and the filling of the tubes with fluid are the main causes of the distressing coughing. This blockage may be due to granulations or stricture, and in many cases both these can be treated through the bronchoscope with considerable relief to the patient. As Jackson has pointed out, the fluid from the lungs is often of such a viscid nature that it cannot be poured out of a reversed test-tube. In fact, when one sees the fluid, one wonders how it is ever coughed

up from the bases of the lungs. Aspiration through the bronchoscope at regular intervals is the only satisfactory method of removing this material, and it helps the patient greatly.

Aspiration helps to avoid the overflowing and flooding of other parts of the lungs mentioned in your leading article. One can picture the fluid being tossed up by the act of coughing, some reaching the pharynx and some falling back into or being driven into other parts of the lungs. Direct aspiration seems to be a much neater process. Lavage through the bronchoscope is not good treatment, but vapours may be introduced.

I am, Sir, yours faithfully,

C. HAMBLEN THOMAS, F.R.C.S.

Harley-street, W., August 25th, 1930.

CARBON DIOXIDE FOAM BATHS.

To the Editor of THE LANCET.

SIR,—It has been our privilege to discuss Foam Therapy with a number of Medical men interested in the Article by Dr. Shillito on Carbon Dioxide Foam Baths published in your issue of June 28th,

With reference, in this connexion, to the Equipment required, may we ask for space in your columns in which to qualify Dr. Shillito's statement when he says: . . . "All that is now required to carry out this treatment is a Foam Distributor obtained either in this Country, *or, more cheaply, Abroad*" . . . &c.

We wish to make it clear that this Company holds British Letters Patent which cover the preparation of a *Double Layer Bath* of Water and Physical Foam. Therefore, any person who produces in England a Double Layer Bath such as Dr. Shillito describes, by other means than a Sandor Distributor (of which we also own the entire British Patent Rights) for the purpose of giving treatment, is thereby infringing these Patent Rights.

It follows that any Doctor who buys Abroad an appliance for the production of a Double Layer Foam Bath, and uses it for giving treatment in his professional capacity in this Country, is equally injuring our Patents.

And so you will see, that when Dr. Shillito informs your readers that they can buy suitable Apparatus Abroad, he is suggesting, unwittingly of course, a procedure which they would not wish to follow when in full possession of the facts.

For your information, we would refer you to British Letters Patent Nos. 305030 and 280208.

We are, Sir, yours faithfully,

for SOAPLESS FOAM LIMITED,

D. CORNFORTH,

Manager.

17–18, Dover-street, London, W. 1., August 22nd, 1930.

MIDDLESEX HOSPITAL.—The 1929 report refers to the lead given by opening beds specially for radiological treatment of cancer. The system of not waking patients before 7 A.M. has been adopted by over 100 hospitals here and in distant lands. More than two-thirds of the reconstruction scheme had been completed at the end of last year, and a number of private rooms for paying patients have already been opened. Building operations reduced the number of beds available, and the in-patients numbered 6607, as compared with 6271 in 1928. This loss of beds increased the cost per head, which was £5 4*s.* 8*d.* against £4 15*s.* 1*d.* in the preceding year. Out-patients numbered 54,400, an increase approaching 2000. In the cancer wing 870 patients were treated, an increase of 158, which, as the number of beds is the same, is accounted for by shorter stays. The individual cost of these patients was £6 6*s.* 11*d.*

STILLBIRTHS AND INFANT MORTALITY.

INTERNATIONAL INQUIRY.

THE inquiry made during 1927–28 by the Health Organisation of the League of Nations[1] into the causes of stillbirths and infant mortality during the first year of life has not been merely into the statistics but into the medical, social, and hygienic aspects of the subject. Investigations were made in Austria, France, Germany, Great Britain, Italy, the Netherlands, and Norway, by methods as far as possible uniform; and since it was impossible that the investigators should attend all confinements in the selected districts, information was obtained through notification by competent authorities, and, in cases of death, by application to the doctor, the midwife, the family, the welfare centre, or any other institution which the mother had attended. The social inquiries were made through the visiting nurse, officials in the registrar's office, clergymen, or other persons well acquainted with the environment of the family, as well as by visits to the home. Information relative to the child's family, the child, and the confinement was obtained by means of a uniform inquiry form which took account of the housing conditions, the morbid history of the family during the life of the child, the obstetric history of the mother, the care and feeding of the infant, the history of the fatal illness, and any personal observations of the investigator.

The infant mortality of the various districts was classified under the headings: low, moderate, high, and very high, and the investigation was made over a period of a year in every case. The investigation in Italy was begun later than elsewhere, and is not included in this analysis.

District Mortality.

Districts with a low infant mortality.—In Great Britain, where the inquiry was conducted by Dame Janet Campbell, a low infant mortality was found in Oxfordshire, and within the same range—3·5 to 4·9 per cent.—fell Hedmark and Oslo West (Norway), and Leiden and Dordrecht (Netherlands). Oxfordshire and Hedmark are both agricultural districts where the housing conditions were found to be poor, the hygienic conditions on the whole favourable, and breast-feeding the usual rule. In Oxfordshire two-thirds of the women received antenatal supervision, but in Hedmark this was rare and child welfare organisation inadequate. Dordrecht, Leiden, and Oslo West, urban districts with a commercial population, shared favourable housing and hygienic conditions, numerous and well-patronised medical institutions and welfare clinics, and a preponderance of breast-fed infants.

A moderate infant mortality—5 to 6·9 per cent.—was found in Croydon and Staffordshire (Great Britain), Breda, Maestricht and Emmen (Netherlands), Lochois and Chinonais (France), Lippe (Germany), and Oslo East (Norway). Rural districts included Staffordshire, Lochois and Chinonais, Lippe, and Emmen, and conditions varied considerably between them; in Staffordshire, for example, the population is semi-agricultural and semi-mining, housing was found to be rather poor, child welfare work well organised, antenatal supervision sought by about one-half the pregnant women, and breast-feeding commoner than artificial. In Lochois and Chinonais, with a wine-growing and agricultural population, and

[1] Memorandum C. H. 820. Obtainable (3*s.* 6*d.*) from George Allen and Unwin, League of Nations Department, 38, Great Ormond Street, London, W.C. 1.

moderate or satisfactory housing and hygienic conditions, child welfare organisation was seen to be little developed and antenatal supervision rare; pregnant peasant women were frequently overworked, but confinements are always conducted by a doctor or trained midwife; breast and artificial feeding maintained equal proportions. In Lippe, also an agricultural district, housing and hygienic conditions are regarded as favourable on the whole, but social conditions often bad; half the female population work, and though antenatal supervision is rare, child welfare organisation is good and breast-feeding common. In Emmen the housing conditions are in places often very bad, and unemployment is prevalent; the birth-rate is high and breast-feeding common, while child welfare and antenatal clinics are only now in the process of organisation. Contrasted with these are the four urban districts with a moderate infant mortality, which show a certain uniformity of conditions. In all except Maestricht the housing conditions are fairly good, and antenatal and child welfare work well organised; breast-feeding was said to be common in all except Croydon.

Districts with a high infant mortality—7 to 9·9 per cent.—included Sunderland (Great Britain), Pays de Caux and Plaisance and the Zone of Fortifications (France), Cassel and Augsburg (Germany), Vienna, districts VI., VII., and VIII. (Austria), and Hoensbrock (Netherlands). Pays de Caux, mainly agricultural, showed bad housing conditions, poorly developed child welfare and antenatal organisations, unskilled midwifery, and defective feeding of infants; Hoensbrock, the other rural district in this group, is devoted chiefly to mining; the housing conditions are favourable, and infant welfare clinics exist but are little used. The remaining districts in this group, all of which are urban, have housing conditions which vary from poor to deplorable, except in Cassel, where they are moderately good, and offer child welfare and antenatal facilities of a high order in all; in the majority of these areas the pregnant women work, in some cases excessively.

A very high infant mortality (10 per cent. and over) was found in Pays de Bray (France), Stelitz (Germany), and Gmunden, Schärding and Engelhartszell, and Vienna, district X. (Austria). All of these, except the Vienna district, are agricultural, and mostly the population shows a low standard of intelligence. Work is common and often excessive among pregnant women, and the child welfare or antenatal centres are either limited or absent, and are seldom well attended; infant feeding is usually defective and frequently artificial; midwifery often reaches a poor standard, and illegitimacy is common. In Vienna, district X. the living and social conditions were found to be bad, and pregnant women often overworked; infant welfare work, however, is well organised.

Principal Causes of Death.

The principal causes of death among infants were classed under digestive disturbances, respiratory diseases, and stillbirth, either due to premature delivery, obstetrical trauma, or some other cause. By far the largest number of deaths were due to respiratory diseases, either as an individual condition or following one of the specific fevers which also played a considerable part in raising the infant mortality. Premature birth, and death from unknown causes were responsible for the highest figures in many districts, while digestive disturbances took a less prominent position in every case. It was found that, in areas where the infant mortality was high, specific infections reached a considerable figure as a cause, while in districts with a low mortality they were practically non-existent.

Conclusions and Recommendations.

The investigators conclude that in districts where the mortality is low and child welfare clinics are abundant and well organised, the incidence of respiratory and infectious diseases and digestive disturbances falls considerably, while the rates for stillbirths and infant mortality during the first weeks of life remain practically the same everywhere. The prevention of stillbirth, they consider, depends largely on efficient antenatal care and the early diagnosis of malpresentations, toxæmias of pregnancy, syphilis, or other conditions which permit of prophylaxis. They therefore recommend the establishment of more antenatal clinics, the supervision of the pregnant woman in industry, and a campaign against the employment of unskilled midwives. They also suggest that financial and other forms of assistance to pregnant women should be extended, so as to permit them to rest during the latter months of pregnancy, and that social measures should be applied impartially to legitimate and illegitimate eldren. The need for more institutional provision and for the more thorough instruction of doctors and midwives in the care of the infant are emphasised; as a preventive measure against digestive disturbances and respiratory and other diseases the extension of child welfare clinics and the better instruction of the public in possible modes of infection are advised.

MEDICAL NEWS

Medical Society of London.

The syllabus for the first half of the 158th session begins with a presidential address on the Stethoscope, Past and Present, by Dr. R. A. Young, to be given on Oct. 13th, following the annual general meeting of the Society. Of the Monday evening discussions that on the prophylactic and therapeutic values of vaccines will be introduced (Oct. 27th) by Sir Almroth Wright; on the diagnosis and treatment of malignant disease of the chest (Nov. 10th) by Prof. Chevalier Jackson; on the pathological conditions of the eye due to inflammatory changes in other parts of the body (Dec. 8th) by Mr. A. F. MacCallan and Mr. Ernest Clarke. Nov. 24th will be a clinical evening. The Lloyd Roberts lecture on Painting and the Healing Art will be delivered on Wednesday, Nov. 19th, by Prof. William Rothenstein, M.A. The Lettsomian lectures next spring are to be given by Dr. J. W. McNee on the Spleen, its Structures, Functions, and Disorders. The annual oration of the Society will be delivered on May 11th, 1931, by Sir John Rose Bradford.

St. George's Hospital Medical School.

On Wednesday, Oct. 1st, at 3 P.M., Lord Riddell will give an inaugural address at the annual prize distribution in the Board Room of St. George's Hospital. Dr. James Collier will take the chair at a dinner to be held on the evening of the same day at the Hyde Park Hotel, Knightsbridge.

Society of Medical Officers of Health.

A provincial meeting of this society will be held at the Grand Hotel, Lowestoft, at 4 P.M., on Friday, Sept. 19th. The subject of discussion will be the Public Health Significance of General Medical Service Schemes, and the speakers will include: Dr. Astley Clarke, senior physician, Leicester Royal Infirmary; Dr. C. E. S. Flemming, member of Consultative Council, Ministry of Health; Dr. H. P. Newsholme, M.O.H. for Birmingham; and Dr. A. M. N. Pringle, M.O.H. for Ipswich. Members will later be entertained to dinner by the Mayor and Corporation of Lowestoft, and on the following afternoon there will be a launch trip on Oulton Broad. Members who intend to be present are asked to notify the executive secretary at 1, Upper Montague-street, Russell-square, London, W.C. 1, by an early post.

Chelsea Clinical Society.

The annual dinner of this society will be held at the Rembrandt Hotel on Tuesday, Oct. 28th, at 7.30 P.M.

Paddington Medical Society.

The next meeting of this society will be held on Tuesday, Sept. 9th, at the Great Western Hotel, Paddington, at 9 P.M., when Dr. E. G. Graham Little, M.P., will give an address entitled Private or Contract Practice?

Royal Sanitary Institute.

The forty-second congress and health exhibition of this Institute will be held at Glasgow from July 4th to 11th, 1931, under the presidency of Sir Henry Mechan.

Radium at Bradford.

The Health Committee of Bradford Corporation has been given official permission to borrow £20,000 for the purchase of radium for St. Luke's Hospital.

King's College Hospital.

The in-patients last year numbered 7006 and cost £10 15*s.* 5*d.* per head; the 41,684 out-patients cost 12*s.* 9*d.* each. The number of patients received into the hospital was the highest since the war. The income was £100,677, and the expenditure £101,821; the debt amounted to £65,867. The annual report refers to the world-wide reputation obtained by the urological department founded in 1922, and to the enormous development of the physical treatment department. A clinic was founded for the investigation and treatment of asthma and allied diseases, and now has more than 100 cases for detailed study.

King's College Hospital Medical School.

This school has now completed a hundred years' work, and an account of this will be given by Dr. Raymond Crawfurd, on Oct. 1st, at the opening ceremony of the winter session, when Dr. G. F. Still will preside. The centenary dinner, at which Sir StClair Thomson will take the chair, will be held on the same evening at the Connaught Rooms. It is proposed to mark the centenary by completing the Medical School buildings as soon as the necessary funds can be collected.

Liverpool Open-Air Hospital for Children.

This hospital at Leasowe, in Cheshire, last year discharged 86·6 per cent. of tuberculous cases "disease quiescent." Of the 110 cases so discharged in 1926, 94 per cent. are now known to be fit; in 1927, 84·8 per cent.; in 1928, 90·6 per cent. An interesting section of the report deals with the 224 cases treated by artificial light. While the results, it is thought, do not prove that artificial light has any specific action upon cases of tuberculous disease, combined general and local irradiation assists and hastens recalcification during convalescence and the healing of sinuses, and shortens the stay in hospital of cases of tuberculous adenitis and peritonitis.

Florence Nightingale Fund.

The annual report states that during the year 78 probationer nurses were admitted from the preliminary training school to the Fund's school at St. Thomas's Hospital, and 51 nurses completed their term of service and were awarded certificates. Miss Lloyd Still, matron of St. Thomas's, and superintendent of the Nightingale Training School, received 1159 applications for the regulations and accepted 163 applicants. From the opening of the school in 1860 to the end of 1929 2434 names were placed on the register of the Nightingale Nurses to be added ultimately to the hospital staff. At the end of the year 37 of these nurses were holding positions as matrons. The income of the fund was £2192 and the expenditure £1988.

Hospital Libraries.

At its conference at Cambridge, from Sept. 22nd to 27th, the Library Association will consider, among other subjects, the provision of libraries for hospitals. Besides a paper on the history and practice of this work in Great Britain, there will be papers from Denmark and the United States. Miss Ostenfeld will read a paper on Collaboration between Public Libraries and Hospitals in Denmark, and will open a discussion on the possibility of applying similar methods in this country. A second paper on the Psychological Value to Patients of Hospital Libraries will be read by Miss Perrie Jones, hospital librarian at St. Paul's, Minnesota, U.S.A. Further particulars may be had from the secretary of the Library Association, 76, Bedford-square, London, W.C. 1.

At the recent Empire Conference of the British Red Cross Society a resolution was passed approving "The Principle of Reading as part of Curative Medicine," and desiring to see it established in all hospitals in due course.

St. Mary's Hospital Medical School.

The annual dinner of past and present students will be held at the Trocadero Restaurant at 7 P.M. on Friday, Oct. 3rd. Dr. Reginald Fuller will take the chair.

New Operating Theatre at Keswick.

Sir John Randles is presenting a new operating theatre, to cost some £4000, to Keswick Hospital. It is to bear the name of Lady Randles.

Oxford Mental Defectives.

Subject to certain consents, Wyfold Court, near Henley-on-Thames, from which Lord Wyfold takes his title, is to be purchased by the Oxford City Council as a home for mental defectives.

Royal Dental Hospital of London.

The prize distribution and conversazione of this hospital and school of dental surgery will be held at the hospital in Leicester-square at 8 P.M., on Thursday, Oct. 2nd. Sir John Rose Bradford, F.R.S., will preside.

A Hunt Hospital Bed.

Mr. H. R. Turner, who has given a bed to the Devonshire Hospital, Buxton, has named it "The High Peak Hunt Bed." Mr. Turner, who is one of the joint masters of the hunt, desires that the bed should be associated with the farmers of the country.

Rebuilding Corbett Hospital.

It is proposed practically to rebuild the Corbett Hospital at Amblecote, Stourbridge, at a cost of £150,000, of which one-third would be provision for maintenance. Between £17,000 and £18,000 has already been subscribed, and it is hoped that substantial assistance will be forthcoming from the John Corbett Trust Fund.

New Doncaster Infirmary.

When the Earl of Lonsdale opened the new Royal Infirmary at Doncaster, he received purses containing more than £4000. The building has cost £156,000, of which £103,000 has been raised; it is the first portion of a scheme for an institution of 300 beds.

Red Cross Clinic for Rheumatism.

The British Red Cross Society's clinic for the treatment of rheumatism (Peto-place, Regent's Park, London, N.W. 1) has been reopened after a month's closure for internal reconstruction. The accommodation has been nearly doubled to meet an unexpectedly large demand. In future, the clinic will be open from 8.30 A.M. to 9.30 P.M., and whereas men and women were formerly treated on alternate days, arrangements have now been made by which both sexes can come on the same day. Since the opening in March about 25,000 treatments have been given, and the attendances have steadily increased. Considerable use has been made of the clinic by private patients, and in July alone over a thousand treatments were given on the private floor. The system of booking appointments for all patients has worked well and will be continued. Five honorary visiting physicians, with 15 clinical assistants, are now at work at the clinic. The remainder of the staff consists of a medical registrar, the sister-in-charge, with sisters-in-charge on each floor to assist her, 15 masseuses, 10 masseurs, and a lady almoner and her assistants. In addition, six new consultants—a dental surgeon, a radiologist, an orthopædic surgeon, a throat specialist, a surgeon, and a gynæcologist—have been appointed. For patients belonging to approved societies a course of nine attendances costs 25*s.*, with subsequent courses if necessary at 20*s.* For private patients treatments cost half a guinea each, in addition to a consultation fee of £2 2*s.* 0*d.* to the consulting physician.

Medical Diary

Information to be included in this column should reach us in proper form on Tuesday, and cannot appear if it reaches us later than the first post on Wednesday morning.

LECTURES, ADDRESSES, DEMONSTRATIONS, &c

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, London, W.

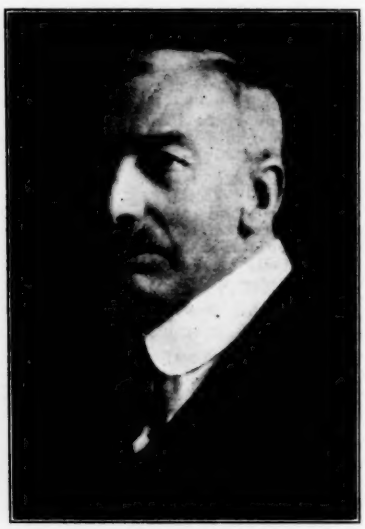
MONDAY, Sept. 8th, to SATURDAY, Sept. 13th.—QUEEN'S HOSPITAL FOR CHILDREN, Hackney-road, Bethnal-Green, E. Special Course in Diseases of Children, occupying all day, with lectures and demonstrations. Syllabus and ticket of admission from the Fellowship of Medicine.

OBITUARY

HERBERT WILLIAM CARSON, F.R.C.S. Eng.

Mr. Carson's death at the age of 59 will be regretted not only by colleagues and collaborators, but by everyone who observed his devotion to post-graduate education and other desirable causes. He was a capable surgeon and a hard worker, and his services to the Prince of Wales's Hospital during the past 30 years were given by mind and heart without stint.

Born in 1870, Carson received his medical education at St. Bartholomew's Hospital, and qualified in 1895. His first appointment was that of house surgeon to the Tottenham Hospital (now the Prince of Wales's) and he returned there as assistant surgeon in 1897. At this time his bent was to towards ear, nose and throat surgery, and he served as clinical assistant at Golden-square, and in the throat department at St. Bartholomew's under Sir Anthony Bowlby before taking charge of this specialty at Tottenham. Meanwhile, in 1899, he had become F.R.C.S. Eng., and was able to throw himself wholeheartedly into the work of his new hospital, and, in due course, of the North East London Post-graduate College. With the late Dr. R. Murray Leslie, Dr. Arthur Giles, and Dr. A. J. Whiting he laid the early foundation of this post-graduate school, which has flourished and widely spread the fame of what was then a small and struggling institution. From the day of the opening, in 1902, he took an active interest in its development and welfare, and until his illness he had a large share in the work. The success of these efforts is evident from the number of graduates who attend for instruction. Both the Admiralty and the India Office recognise the College for purposes of study leave.



MR. CARSON.
[Photograph by Elliott and Fry.

Partly by way of sequel came the association and coöperation of the smaller general and special hospitals of London in post-graduate teaching under the Fellowship of Medicine. The grouping was based on a report and list prepared by the Tottenham group for the Athlone Committee, and during the greater part of the succeeding ten years Carson played an energetic part in the work of the Fellowship. This was arduous and often delicate. For many years he was unofficial honorary secretary for overseas, and in this capacity visited Canada in order to inform himself of the needs of medical men from the Dominions. Latterly he was chairman of the executive committee of the Fellowship, and kept things moving by the impetus of his progressive personality. Recently he was appointed to the provisional organisation committee of the new British Post-graduate Hospital and Medical School at Hammersmith.

As a surgeon, Carson's work was chiefly concerned with the abdomen, but his interests remained general. He was the editor of—and a large contributor to—"Modern Operative Surgery," published in 1924. This appeared in two volumes and its design was to exclude operations which have lost their usefulness, even if they are classics. In its preparation he secured the services of the younger generation of surgeons and by enforcing the rule he produced a valuable book within a reasonable compass. He also edited the tenth edition of Pye's "Surgical Handicraft." In the medical societies he was a frequent speaker and displayed the same lucidity as in his teaching. At various times he held the presidency both of the Hunterian Society and the Medical Society of London, and to these as to other offices he brought enthusiasm and well-directed labour. In 1929 he travelled to America to deliver the Mütter Lecture of the College of Physicians of Philadelphia, taking Intestinal Obstruction as his subject, and treating it exhaustively from the historical, clinical, and operative points of view. During the late war, he held a captain's commission in the Royal Army Medical Corps and served as surgeon to the King George Hospital.

Mr. Carson was married, but had no family. In leisure time he was a chess player, a keen cricketer, and a seafarer in small sailing boats. In person he was tall, well-built, soft of voice, and rather deliberate of utterance, and he had the gift of making friends. Dr. A. J. Whiting as one of his colleagues at the Prince of Wales's tells us that it is not too much to say that Carson lived for the hospital. "In all discussions of policy and procedure the crucial point with him was—what is best for the hospital? To those who know, or can read between the lines, it will be enough to say that he took an active part, or even a leading part, in two enlargements of the place, and was plunged in a third at the time of his death. Impetuous, genial, sometimes rather ruthless, but with a well of tenderness not far from the surface, he focused his attention on the object of attainment rather than the foreground. But if he was forceful he was also lovable.

"He will be remembered not so much as a good surgeon or a good hospital colleague, although he was both of these, or as an excellent teacher, and he was that; but rather as a man of vivid personality and a stark worker. He manifested to all, without any possibility of doubt, that the Prince of Wales's Hospital implied for him the Prince of Wales's motto."

CHARLES BUTTAR, M.D., D.P.H. Camb.

Dr. Buttar who died after an operation at Limecroft, Guildford, on August 31st, was the son of Charles Buttar of Elgin Crescent, Notting Hill, by Emily, daughter of James Lovett, of Cricklade, Wilts. He was born in 1867 and was educated at Westminster School and Pembroke College, Cambridge. In 1887 he gained a second class in the Classical Tripos and in 1889 he graduated, after obtaining a second class in

Part I. of the Natural Science Tripos. He then proceeded to St. Bartholomew's Hospital and qualified in 1892, taking the M.B. and B.Chir. Camb. in the same year. In 1896 he proceeded to the M.D., having been admitted M.A. in 1893 and taking a D.P.H. in 1895. At St. Bartholomew's Hospital he served as house surgeon for a year and was for a time assistant anæsthetist, after which he was appointed house surgeon to the Metropolitan Hospital, subsequently becoming clinical assistant at the Western Ophthalmic Hospital.

For many years Dr. Buttar carried on a large practice in Notting Hill and Kensington, living latterly at Inverness-terrace until he retired to Felstead in Essex. So long as he lived in London he took an active part in the affairs of the British Medical Association and being a first-rate organiser and an excellent man of business, he acted during the war as chairman of the Executive Committee of the Central Medical War Committee, a body which was entrusted with the delicate duty of deciding which members of the medical profession could be spared for duty abroad; when the medical needs of the Army and Navy were at their greatest there was a dangerous depletion of the medical men required to serve the country at home. The Committee over which he presided, which was charged to hold the balance, had no acuter or fairer member than its chairman. The same qualities of tact and discretion were displayed at the Harveian Society, where he was in succession secretary, vice-president, president in 1909, trustee and treasurer. He found the finances of the Society in a bad state, but his energy and capacity enabled him to hand over the treasurership to his successor Dr. G. de Bec Turtle in the flourishing condition in which they have since been maintained.

Dr. Buttar was also an active member of the Council of Epsom College. He married in 1898 and had one son.

JOHN THOMSON WILSON, M.D., D.P.H. Aberd., J.P.

Dr. J. T. Wilson died on August 20th at his home in Bothwell, Lanarkshire, at the age of 75. He had retired on grounds of health some years ago but maintained his interest in medical affairs.

A native of Cambuslang, in Lanarkshire, Wilson graduated in medicine at Aberdeen in 1891 and proceeded to the M.D. degree five years later, with a thesis on the Natural History of Scarlet Fever. This was an elaborate and valuable statistical study and its general conclusion that preventive measures have little effect in limiting the disease has been, on the whole, verified. After serving as assistant medical officer in Shropshire for two years he was appointed county medical officer for Lanarkshire in succession to the late Dr. James McLintock, who in 1894 became the first medical member of the Local Government Board for Scotland. Lanarkshire is the biggest Scottish county, with a population of about 300,000 rural and about 200,000 urban. Since Dr. Wilson's appointment Glasgow has annexed some of it, but the county still remains the largest.

In the course of his long career as medical officer Wilson commanded great influence because of his passionate sincerity. He displayed a deep earnestness in all that he undertook—which was a great deal. He organised his great department on lines to suit the developments of the future and the county is to-day reaping the benefit of his foresight. To any student of the health movement in the Northern Kingdom his elaborate annual reports were indispensable. Apart from these he produced two other striking pieces of work—namely, special reports on rivers pollution and on the housing of miners. The latter was one of five required by the Local Government Board as a preliminary to the work of the Royal Commission on Housing. All were excellent for their counties, but Wilson made his report both a groundwork for recommended reforms and an administrative survey of the whole mining area. It was of great use to the Royal Commission when members visited the numerous miners' rows and villages of Lanarkshire. The report showed what ought to have been done; the visit of inspection showed what had not been done. But the county has made up leeway and it would be difficult to name any place in Great Britain where, relatively, greater progress has been made. His devoted work over 30 years has ended in a body of institutions that any county may be proud of. Among them may be mentioned the Hairmyres Sanatorium and Work Colony established during his term of office.

Wilson was a scholar in the academic sense and he carried the detail of his work easily; but he felt very keenly the serious responsibility of the position. In addition he took his full share in the work of the Royal Sanitary Association of Scotland, the Society of Medical Officers of Health, and other bodies and held examinerships at Aberdeen and Edinburgh Universities.

Dr. Wilson's wife survives him.

Appointments

ADAM, JAMES R., M.B., Ch.B. Edin., D.P.H. Edin. and Glas., has been appointed Medical Officer of Health for the county of Roxburgh.

BROWNLIE, JAMES LAW, M.D., Ch.B. Glasg., D.P.H. Camb. (at present County Bacteriologist and Pathologist in Lanarkshire), has been appointed a Medical Officer of the Department of Health for Scotland.

DUGAN, ALEXANDER M., M.B., Ch.B. Aberd., D.P.H. Aberd., has been appointed Assistant Medical Officer of Health for School Medical Services in Aberdeen.

THOMAS, ALFRED TREVOR GWYN, M.B., B.S. Durh., has been appointed one of the Surgeons on the *Mauretania*.

Certifying Surgeons under the Factory and Workshop Acts: AITKEN, J. (Wainfleet District of the County of Lincoln); COXON, H. C. (Newburn District of the County of Northumberland); CREASER, F. G., M.B., B.Ch. Edin. (Snaith District of the County of York, W.R.); THOMSON, G. L., M.B., Ch.B. Glasg. (Tighnabruaich District of the County of Argyll).

Vacancies

For further information refer to the advertisement columns.

Albert Dock Hospital, Connaught-road.—M.O. At rate of £110.
All Saints' Hospital for Genito-Urinary Diseases, Vauxhall Bridge-road, S.W.—H.S. At rate of £150.
Ascot, Heatherwood Hospital.—Res. Asst. M.O. £300.
Barnsley, Beckett Hospital and Dispensary.—Jun. H.S. £140.
Bath, Royal United Hospital.—Asst. H.S. At rate of £120.
Bedford County Hospital.—H.S. £175. Also Asst. H.S. £130.
Birmingham General Hospital, Anæsthetist.—£120. Also three H.S.'s. £70.
Birmingham, Selly Oak Hospital.—Cas. O. £200.
Bradford City.—Asst. Bacteriologist. £600.
Brighton, Royal Sussex County Hospital.—Cas. H.S. £120.
Bristol Royal Infirmary.—Asst. for Cancer Research Laboratories. £400.
Cambridge, Addenbrooke's Hospital.—H.S. Also H.S. to Special Depts. Each at rate of £130.
Cancer Hospital, Fulham-road, S.W.—H.S. At rate of £100.
Cardiff, King Edward VII. Welsh National Memorial Association.—Area Asst. Tuberculosis Phys. £600. Also half-time Asst. Tuberculosis Officer for Pontypridd area. £300.
Cardiff Royal Infirmary.—Gynæcological H.S.—At rate of £50.
Central London Throat, Nose, and Ear Hospital, Gray's Inn-road, W.C.—Hon. Asst. Anæsthetist.
Chesterfield and North Derbyshire Royal Hospital.—H.S. At rate of £100–£175.
Connaught Hospital, Orford-road, E.—H.P. At rate of £150.
Derby, Derbyshire Hospital for Sick Children.—Res. M.O. At rate of £150.

Dewsbury, New Dewsbury and District General Infirmary.—Jun. H.S. £150.
Dreadnought Hospital, Greenwich.—H.P. and H.S. Each at rate of £110.
Dulwich Hospital, East Dulwich-grove, S.E.—Third Asst. M.O. £300.
Eastcote, Middlesex, St. Vincent's Orthopædic Hospital.—Res. M.O. At rate of £150.
East Ham Memorial Hospital, Shrewsbury-road, E.—Res. M.O. At rate of £200. H.P. At rate of £150. H.S. At rate of £120.
Evelina Hospital for Children, Southwark, S.E.—H.S. At rate of £120.
Glasgow University.—Dr. Robert Pollok Lectureship in Materia Medica and Therapeutics.
Gloucester, Gloucestershire Royal Infirmary and Eye Institution.—Second H.S. At rate of £120.
Great Yarmouth General Hospital.—Sen. and Jun. H.S.'s. £150 and £140 respectively.
Guildford, Royal Surrey County Hospital.—H.S. £150.
Guy's Hospital Dental School, London Bridge, S.E.—Teacher of Conservative Dental Surgery. £1000.
Halifax Royal Infirmary.—3rd. H.S. £150.
Hospital for Tropical Diseases, Endsleigh-gardens, W.C.—Two H.P.'s. Each at rate of £150.
Ilford, King George Hospital.—Res. M.O. £250. Also House Officer. £100.
Infants Hospital, Vincent-square, Westminster.—Two H.P.'s. Each at rate of £75.
Inverness District Mental Hospital.—Jun. Asst. M.O. £350.
Ipswich, East Suffolk and Ipswich Hospital.—Cas. O. £150. Also H.S. At rate of £120.
Kingston-upon-Hull, City and County of, Beverley-road Institution.—Asst. M.O. £300.
Lanark, County of.—Bacteriologist and Pathologist. £750.
Lancashire County Council.—Asst. County M.O. £800.
Lancaster County Mental Hospital.—Asst. M.O. £350.
Leeds Public Dispensary.—Jun. Res. M.O. £150.
Liverpool and District Hospital for Diseases of Heart.—H.P. At rate of £52.
Liverpool Royal Children's Hospital.—Second Res. M.O. At rate of £120.
Liverpool Stanley Hospital.—H.P. and H.S. Each £100.
London Female Lock Hospital, 283, Harrow-road, W.—H.S. £150.
London Hospital, E.—Surgical First Asst. and Registrar. Also Medical First Asst. and Registrar. Each £300.
London Lock Hospital, 91, Dean-street, W.—H.S. At rate of £200. Also Two Surg. Regs. Each £100.
Macclesfield General Infirmary.—Res. H.S. At rate of £180.
Madras, Medical College, Vizagapatam.—Professor of Pathology. 1100 Rs. per month.
Manchester, Ancoats Hospital.—H.S. At rate of £100.
Manchester and Salford Hospital for Skin Diseases.—H.S. £100.
Manchester, Baguley Sanatorium.—Asst. M.O. £350.
Manchester, Royal Children's Hospital, Gartside-street.—Two Asst. M.O.'s. At rate of £150.
Manchester, Royal Children's Hospital, Pendlebury.—Res. M.O. and Res. Surg. O. At rate of £125.
Manchester Royal Infirmary, Roby-street.—Jun. H.S. and Cas. O. £100.
Merthyr General Hospital.—Res. H.S. At rate of £150.
Miller General Hospital, Greenwich-road, S.E.—Cas. O. At rate of £150. Also H.P. and H.S. Each at rate of £125.
National Hospital, Queen-square, W.C.—Res. M.O. £200.
Northampton General Hospital.—H.P., 2 H.S.'s, and 2 Asst. H.S.'s.—All at rate of £150.
Nottingham Children's Hospital.—Res. H.S. At rate of £150.
Nottingham General Hospital.—H.P. Also 2nd Cas. O. Each at rate of £150.
Oldham Royal Infirmary.—Two H.S.'s. Each at rate of £175.
Park (Fever) Hospital, Hither Green, S.E.—2 Asst. M.O.'s. Each £500.
Plymouth, South Devon and East Cornwall Hospital.—Asst. Pathologist. £350.
Preston and County of Lancaster Royal Infirmary.—H.S. At rate of £150.
Princess Louise Kensington Hospital for Children, St. Quintin-avenue, N. Kensington, W.—H.S. and Cas. O. At rate of £75. Also Hon. Physician and Hon. Radiologist.
Reading, Royal Berkshire Hospital.—Cas. O. and Res. Anæsthetist. Each at rate of £150.
Royal Dental Hospital of London, Leicester-square, W.C.—Asst. Dental Surgeon.
Royal Eye Hospital, St. George's Circus, S.E.—12 Salaried Refractionists, 12 Clinical Assts., and 1 Pathologist.
Royal National Orthopædic Hospital.—H.S. At rate of £150.
Royal Northern Hospital, Holloway, N.—H.P., Res. Out-Patient Cas. O. and Anæsthetist. Each at rate of £70.
Ryde, Royal Isle of Wight County Hospital.—Vacancy on Hon. Med. Staff. Also Res. H.S. £180.
St. Bartholomew's Hospital, E.C.—Asst. Surgeon for Diseases of Throat and Nose. Also Asst. Surgeon to Orthopædic Dept.
St. Helen's Hospital.—H.S. £250.
St. Mary Abbots Hospital, Marloes-road, Kensington, W.—Asst. M.O. £250.
St. Mary's Hospital, W.—Physician in charge of Out-Patients.
St. Peter's Hospital for Stone, &c., Henrietta-street, Covent Garden W.C.—H.S. At rate of £75.
Salford Royal Hospital.—Two H.S.'s Each at rate of £125.
Sheffield Royal Hospital.—Res. H.S. Also Res. Anæsthetist. Each at rate of £80.
Shrewsbury, Eye, Ear and Throat Hospital.—H.S. £200.
Southampton Children's Hospital and Dispensary for Women.—Res. M.O. At rate of £100.
Southampton, Royal South Hants and Southampton Hospital.—Asst. H.S. At rate of £180.
South London Hospital for Women, South Side, Clapham, S.W.—H.P. and H.S. Each at rate of £50.
South Shields, Ingham Infirmary.—Jun. H.S. £150.
Stafford, Staffordshire General Infirmary.—H.S. and H.P. At rate of £200 and £150 respectively.
Stoke-on-Trent, North Staffordshire Royal Infirmary.—Asst. H.P. At rate of £125.
Swansea Hospital.—H.S. £150.
Talgarth, Breconshire, Mid-Wales Counties Mental Hospital.—Asst. M.O. £350.
Tilbury Hospital, Essex.—H.S. At rate of £150.
Tynemouth, County Borough of.—Asst. M.O.H. £540.
Uxbridge, Middlesex, Hillingdon Institution.—Res. M.O. £600.
Victoria Hospital for Children, Tite-street, Chelsea, S.W.—H.S. At rate of £100.
Walsall General Hospital.—H.S. At rate of £150.
West London Hospital, Hammersmith-road, W.—H.P., Two H.S.'s., and Res. Anæsthetist. Each at rate of £100.
West Lothian, Bangour Mental Hospital.—Second Asst. M.O. £350.
Westminster Hospital Annexe, 66, Fitzjohn's-avenue, Hampstead.—Jun. H.S. At rate of £104.
Willesden Municipal Hospital.—Res. M.O. £250.
Wolverhampton and Midland Counties Eye Infirmary.—H.S. £150.
Woolwich and District War Memorial Hospital, Shooters Hill, S.E.—H.S. At rate of £100.

The Chief Inspector of Factories announces a vacancy for a Certifying Factory Surgeon at St. Margaret's Hope (Orkney).

Births, Marriages, and Deaths

BIRTHS.

AVERY.—On Aug. 25th, the wife of Dr. Harris Avery, of a daughter.

CANE.—On August 23rd, at Reepham, Norfolk, the wife of Dr. Maurice H. Cane, of a daughter.

KERRIGAN.—On Aug. 23rd, at Horrabridge, the wife of Surgeon-Commander O. J. M. Kerrigan, R.N., of a son.

LLOYD.—On August 18th, at Avenue-road, Regent's Park, the wife of Eric Ivan Lloyd, F.R.C.S., of a daughter.

SPEIRS.—On Aug. 26th, at Walker-street, Edinburgh, the wife of Dr. R. C. Speirs, Tanganyika Medical Service, of a daughter.

WHAMOND.—On August 19th, at Bentinck-street, W, the wife of Captain W. D. Whamond, West African Medical Service (Royal Army Medical Corps, retired), of a son.

MARRIAGES.

STEWART—DOS SANTOS.—On August 12th, at Knockbreda Parish Church, Belfast, H. Hilton Stewart, M.D., M.R.C.P. Lond., to Clara Maria Luiza, daughter of the late Mr. Antonio Luiz dos Santos and Mrs. dos Santos, of Rio de Janeiro, Brazil.

WRIGHT—SHELDON.—On August 30th, at St. Andrew's Church, Cheltenham, Lieut.-Colonel Robert E. Wright, C.I.E., I.M.S., M.D. Dub., to Ruby E. Sheldon, daughter of Dr. S. T. Pruen, Cheltenham.

DEATHS.

AYTOUN.—On Aug. 28th, at Zermatt, Switzerland, while on holiday, James Aytoun, B.Sc. (Hons.), L.R.C.P., M.R.C.S., only son of Dr. and Mrs. Aytoun, Broadstairs, Kent, aged 23.

BALL.—On August 23rd, at Park-terrace, Oxford, John Augustus Ball, M.B. Lond., in his 88th year.

BEVERLEY.—On August 31st, at Overstrand, Norfolk, Michael Beverley, M.D. Edin., M.R.C.S. Eng., L.S.A., J.P., in his 89th year.

BUTTAR.—On Aug. 31st, following an operation, Charles Buttar, M.D., of Guildford, and formerly of Inverness-terrace, W.

CARSON.—On August 31st, Herbert W. Carson, F.R.C.S. Eng., of Harley-street, Senior Surgeon, Prince of Wales's General Hospital, Tottenham, in his 60th year.

DOWN.—On Aug. 26th, at Whitchurch, Devon, Elgar Down, M.D. Durh., F.R.C.S. Edin., late of Plymouth, aged 63.

FINIGAN.—On Aug. 29th, Daniel O'Connell Finigan, M.D. Berlin, M.R.C.P. Lond., M.R.C.S. Eng., of West Southbourne, formerly of Fordingbridge, aged 55.

HIGGINS.—On August 22nd, at the Shaftesbury Hotel, Liverpool, William Robert Higgins, M.D., F.R.C.S., of Bridge-street House, Louth, Lincolnshire.

KENT.—On August 18th, at a nursing home, Sydney Kent, M.B., B.Chir.Camb., of The Corner House, Bexhill-on-Sea, aged 65.

LITTLEJOHN.—On Aug. 27th, at Southwold, from heart failure while bathing, Thomas Plested Littlejohn, M.R.C.S., L.R.C.P. Lond., of Leigh-on-Sea, Essex.

MARTIN.—On Aug. 27th, at Atherton, near Manchester, Major William Young Martin, M.B., Ch.B. Viet., late R.A.M.C. (T.), aged 50.

SEYMOUR.—On August 18th, at his residence, Ambrose-avenue, Golders Green, George Seymour, L.D.S. Eng., of West End-lane, N.W., aged 68.

TUKE.—On August 20th, at The Limes, Sutton Valence, Maidstone, George Montague Tuke, M.R.C.S., J.P.

N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages and Deaths.

NOTES, COMMENTS, AND ABSTRACTS

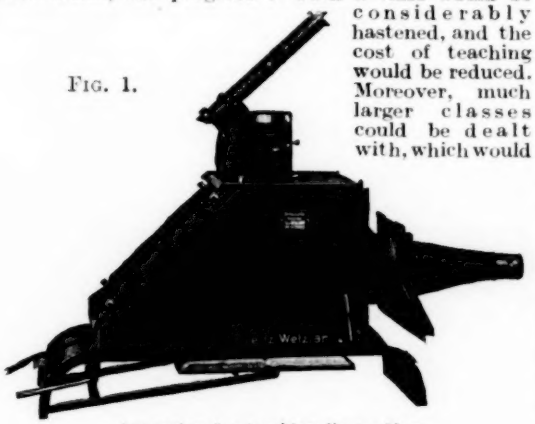
AN APPARATUS FOR TEACHING LIP-READING TO LARGE AUDIENCES.

By Charles M. R. Balbi, A.M.I.E.E.,
Hon. Consulting Electrical Adviser to the National Institute for the Deaf.

Of the various available means of thought transference for the stone deaf lip-reading is by far the most valuable, but it is essential that the "listener" keeps a minute observation of the speaker's lips, which at any distance is difficult. The conventions of the deaf and dumb alphabet are still the most reliable means of intercommunication for the deaf, but this system is useless when a deaf person wishes to communicate with a person who has no knowledge of the deaf and dumb code. Further, the language of signs stamps the user as deaf, and the self-conscious person does not always care to give himself away by an attempt at this sort of conversation. The next best method is perhaps writing, but the exchange of written messages is cumbersome, and involves time. A third method of hearing through the sense organs of touch and vibration, vibrations being transmitted through special "filter circuits" to a special receiver, has been evolved by Mr. Robert H. Gault.[1] This method does not seem to have been able to compete with the natural one of lip-reading, and hence it is desirable to encourage this art where possible.

Lip-reading is usually taught individually, or if it is taught in a class, each learner has the individual attention of the teacher for a few moments. This is advisable because, as already stated, it is essential for the pupil to watch the speaker closely. If it were possible to avoid this concentration on individuals, the progress of such a class would be considerably hastened, and the cost of teaching would be reduced. Moreover, much larger classes could be dealt with, which would be of great benefit to the deaf, since there is a great shortage of teachers of lip-reading.

Fig. 1.

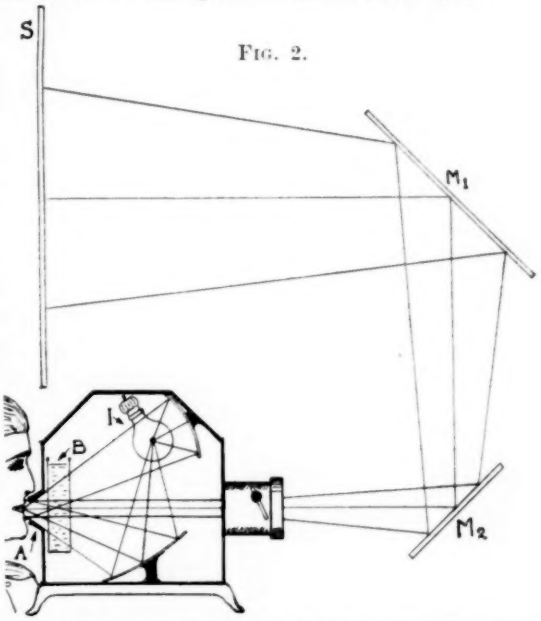


Apparatus for teaching lip-reading.

The apparatus by which I have found it possible to fulfil these requirements is very simple; it consists merely of a conveniently constructed epidiascope, which has hitherto been used for reflecting illustrations of books and specimens. With an apparatus kindly lent to me by Messrs. Leitz and Co., ample proof was afforded that a teacher will be able to instruct a large class; the movement of the teacher's lips is reflected on to a screen and its area is enlarged many hundredfold, and is easily followed from a distance. The apparatus on which my experiments were conducted (see Fig. 1) was not designed for reflecting parts of the living body; the face of the speaker being so near the source of light is subjected to an intense light and heat, the effect of the heat being particularly disagreeable. With a larger (and hence more expensive) lens, the speaking distance from the source of light can be lengthened. This permits an alum bath to be inserted to absorb the radiant heat; the conducted heat is also much reduced at the greater distance, and the discomfort of the speaker would be abolished.

[1] See Franklin: Inst. Jour., September, 1927, p. 329.

Fig. 2.



An optical system designed for enabling a large number of persons to lip-read from one source. A = aperture. B = alum bath. I = illuminating source. M_1 and M_2 = mirrors. S = screen.

Fig. 2 represents an optical system in which the disadvantages have been overcome. Study of the reflected image shows that the speaker's face will appear in vertical position, enlarged, but with the left side of the face transposed to the right and vice versa; but since the face is symmetrical, or sufficiently so for the purpose, the transposition does not affect those who are learning to read the movements thrown on to the screen. The mirrors (M_1 and M_2) can be placed at the back of the apparatus, and the screen (S) can be made of ground glass or some transparent material. The teacher speaks into the aperture A in the ordinary way, and the movements of his lips, which are reflected on the screen, are protected from the rays of the illuminating source I by the alum bath B. If it were decided to manufacture such an apparatus it should be possible to market it for about £100. In view of the saving in the teacher's time the question should be well worth considering. The apparatus could be used not only in schools but also in churches and lecture halls when the audiences are deaf.

BLENORETTES.

We have received from Medical Accessories, Ltd., 92, Baker-street, London, W., a simple device which is intended to take the place of the unsatisfactory gonorrhœa bag. Blenorettes are cone-shaped waterproof reservoirs for fitting over the glans and are retained in place by zinc oxide plaster strips. Beyond a perforated felt-like disc the cones are filled with antiseptic gauze. Among the advantages claimed for this appliance are ease of application, firm fixture, and non-obstruction of the flow of discharge. The tips of the plaster strips are non-adhesive so as to facilitate removal.

"AN OFFICIAL CORRECTION FROM THE M.R.C."

To the Editor of THE LANCET.

SIR,—In your issue of August 16th (p. 361) you give prominence to an official statement by the Medical Research Council under the above title. The Council complain that misuse has been made of their name in a statement issued by our American house which reads as follows:—

"The Pharmaceutical Society of Great Britain, after consultation with the Medical Research Council, adopted Gynergen as the standard for ergot."

I am directed by Sandoz Chemical Works, Basle, to request the courtesy of your columns to reply to the communication of the Medical Research Council, which is presented in such a manner that it fails to reveal the whole truth. It should be made clear that Gynergen is ergotamine tartrate, and that there is only one ergotamine—viz., Ergotamine, Stoll-Sandoz.

You have already published at my request an extract from the *Pharmaceutical Journal* of Feb. 20th, 1926 (see THE LANCET, August 23rd, p. 410). Further, in the same journal for March 13th, 1926, the following appeared:—

"In the number of this journal, published on Feb. 20th last, a description appeared of the tests which these laboratories are prepared to carry out. When a preparation has been tested, a certificate is issued, which in the case of satisfactory preparations may be used by the maker as the basis of a statement on the label. . . . The statement appearing on the label must be confined to the words . . ." "(6) In the case of ergot perparations, c.c. of this preparation contains 1 mgm. ergotamine as determined by a biological test carried out by the Pharmaceutical Society of Great Britain."

To make the matter more clear we quote from the *Pharmaceutical Journal* of May 14th, 1927, where the Director of the Pharmacological Laboratories, replying to Mr. A. O. Bentley, stated: "There has been no ergotoxine in this country since the war until a month or two ago."

The reasons which caused the substitution of a salt of an amorphous alkaloid, difficult to purify, of lesser stability, less soluble, and which can only be conserved with difficulty (in vacuo over phosphorus pentoxide) for a definite, pure, stable, crystalline substance (base as well as salt) are probably not relevant here, but it is clear that ergotamine tartrate *was* adopted as a standard for ergot preparations, and that the Medical Research Council *was* consulted.

I am, Sir, yours faithfully,

"Sandoz" Scientific and Research Department, August 25th, 1930. J. FLINT, Manager.

THE LANCET has been asked by the Director of the Pharmacological Laboratories, Pharmaceutical Society of Great Britain, to publish the following note: "With reference to the extract from the *Pharmaceutical Journal* of Feb. 20th, 1926, published by you, at the request of the Sandoz Chemical Works, in THE LANCET for August 23rd, it should be realised that the statement was superseded by the announcement in the paper by Burn and Ellis, published in the *Pharmaceutical Journal*, 1927, vol. cxviii., p. 384, that 'Ergotoxine phosphate has been adopted as a standard for ergot.' A copy of this paper was forwarded to the Manager of the Pharmaceutical Department, Sandoz Chemical Works, 5, Wigmore-street, on June 8th, 1927, and I have his acknowledgement of its receipt."

HAY-FEVER.

A BOOK by Dr. R. M. Balyeat,[1] now in its third edition, tells the familiar story of protein sensitisation, and tells it avowedly to the patient rather than to the profession. It gives the life history, with illustrations, of such substances incidental to the asthma story as kapok and orris; it gives illustrations too, of a horse, a cat, some dogs, and so on—even a young woman looking into a looking glass to illustrate the use of orris. In short, the layman will find the book light reading, and need not be deterred by fear of finding it too scientific or technical. Some of the explanations of technicalities will probably seem naive, even to readers little versed in technical nomenclature. For example: "The terms 'cutaneous' and 'dermal' will frequently be used. They refer to the skin." It would be heavy handed to criticise the book too strictly from the angle of the pathologist, but it seems a pity to use the term "hay-fever" for any paroxysmal rhinorrhœa, whether caused by grass pollen or not.

[1] Allergic Diseases: Their Diagnosis and Treatment. By Ray M. Balyeat, M.D., of Oklahoma City. Philadelphia: F. A. Davis Co. 1930. Pp. 395. $5.

THE DUTCH PESSARY.

To the Editor of THE LANCET.

SIR,—The recent correspondence on the Dutch cap raises the important point of uniformity of standard in fitting. Where the Dutch pessary is used, in a suitable case, the Walworth technique is based on the view that the maximum occlusion of the vagina is the object of its use, provided there is no harmful or uncomfortable pressure. The size of the cap is determined by the capacity of the vagina in question. The average size of the cap used at Walworth (where most of the cases are mothers with several children) is 72½.

The rim of the cap rests behind the pubic bone in the anterior fornix, and posteriorly, its exact position is largely determined by the length of the cervix, a short, high cervix permitting the rim to be tucked away into the posterior fornix.

The essential points in the use of this pessary are: (*a*) that the rim should be in contact with the vagina walls throughout its circumference; (*b*) that it should not be dislodged by moderate increase of intra-abdominal pressure, such as coughing and straining; (*c*) that it should be perfectly comfortable to the wearer. The spermaticide commonly used at Walworth (where most of the patients are very poor) is a lactic acid ointment, which is cheap, and serves also as a lubricant. In addition, douching before and after removing the cap with soapy water is part of the routine. Where for certain reasons douching is inadvisable, a soluble spermaticide (semori, lactic acid, &c.) is recommended in addition to the spermaticidal ointment.

Obviously, there are many cases where the Dutch pessary is unsuitable, such as lax vaginal walls and damaged perineum, prolapsed uterus, the presence of a ring or Hodge pessary, and severe constipation (patients are warned not to use the pessary when they are constipated). In some cases which are otherwise quite suitable, there is no adequate space in the anterior fornix in which the rim of the pessary can be fixed.

We are, Sir, yours faithfully,

LILY C. BUTLER,
GLADYS M. COX,
Medical Officers, Walworth Women's Welfare Centre.

August 30th, 1930.

LONDON CHARITIES.

WE have received a copy of the thirty-eighth edition of the Annual Charities Register and Digest,[1] which, as everyone knows, is a classified register of charities in or available for the metropolis. Little alteration has been made in this edition except to bring the subject matter scrupulously up to date, and the index is a model of completeness and convenience. As on previous occasions the attempt has been made to include only bona fide institutions and societies, but the preface contains the usual warning that the entry of an institution in the register or in its advertising pages is not equivalent to a general recommendation of it. The editor solicits particulars of institutions which are not mentioned in the present issue; these should be sent to him at Denison House, Vauxhall Bridge-road, London, S.W.

[1] London: Longmans, Green and Co., and Charity Organisation Society. 1930. Pp. 553. 8*s*. 6*d*.